Dissertation on

A COMPARATIVE STUDY ON THE FASTING AND POST PRANDIAL LIPID LEVELS AS A CARDIOVASCULAR RISK FACTOR IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

Submitted in partial fulfillment of requirements of

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CERTIFICATE FROM THE DEAN

This is to certify that this dissertation entitled ***"A COMPARATIVE STUDY ON THE FASTING AND POST PRANDIAL LIPID LEVELS AS A CARDIOVASCULAR RISK FACTOR IN PATIENTS WITH TYPE 2 DIABETES MELLITUS"****is the bonafidework of* ***Dr.DEEPA KP****in partial fulfillment of the university regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, for M.D General Medicine Branch I examination to be held in April 2017.*

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DECLARATION

I, ***Dr.DEEPA K P****declare that I carried out this work on* ***"A COMPARATIVE STUDY ON THE FASTING AND POST PRANDIAL LIPID LEVELS AS A CARDIOVASCULAR RISK FACTOR IN PATIENTS WITH TYPE 2 DIABETES MELLITUS****"at the Department of Medicine, Govt. Rajaji Hospital during the period March2015 to August2016. I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree or diploma to any other University, Board either in India or abroad. This is submitted to The TamilnaduDr.M.G.R.Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D degree examination in General Medicine (Branch I) to be held on April 2017.*

Place : Madurai *DrDEEPA K P*

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CONTENTS

ABBREVIATIONS

ADA	—	American Diabetes Association
T2DM	---	Type2 Diabetes Mellitus
BMI		Body Mass Index
BP		Blood Pressure
CAD	—	Coronary Artery Disease
WHR	---	Waist Hip Ratio
TC	---	Total Cholesterol
CKD		Chronic Kidney Disease
CVA	—	Cerebro Vascular Accident
PAF	---	Platelet activating factor
DM		Diabetes Mellitus
ECG	-	Electrocardiogram
FBS		Fasting Blood Sugar
WHO		World Health Organisation
AGE	---	Advanced glygosylation End Product
GDM	—	Gestational Diabetes Mellitus

LDL		Low Density Lipoprotein
HR		Heart Rate
HT	-	Hpertension
IGT		Impaired Glucose Tolerance
MI		Myocardial infarction
VLDL		Very Low Density Lipoprotein
PPBS	—	Postprandial Blood Sugar
HDL		High Density Lipoprotein
RFT		Renal Function Tests
IDL		Intermediate Density Lipoprotein
IFG		Impaired fasting Glucose

INTRODUCTION

INTRODUCTION

The pandemic of Diabetes mellitus poses public health challenge for every country especially as WHO projected DM will be the 7th leading cause of death in 2030.

Overall, cardiovascular disease, which includes coronary artery and cerebrovascular disease, accounts for 65% of all deaths among persons with diabetes While traditional risk factors play an important role in the development of atherosclerosis in subjects with diabetes, the rate of cardiovascular mortality and morbidity in persons with diabetes exceeds by 50% the rate predicted by these risk factors

Diabetes mellitus is a major independent risk factor for cardiovascular disease (CVD) The central obesity strongly related to insulin resistance and contributes to this pathogenesis through an increase in visceral adipocytes. Excess abdominal fat ,assessed by measurement of waist to hip ratio,is independently associated with a higher risk for cardiovascular disease.

Diabetic dyslipidemia consist of elevated triglyceride ,low HDL,and an increased proportion of small dense LDL.The high cardiovascular mortality which is associated with Type 2 DM is due to a prolonged, exaggerated, postprandial state.

The abnormal lipid profile in the postprandial state is more significant than the abnormal lipid profile in the fasting state in causing atherosclerotic complications in Type 2 diabetics

In this study, an effort is made to correlate and assess the significance of post prandial dyslipidemia with respect to fasting dyslipdemia as cardiovascular risk factor in these patients.

AIMS AND OBJECTIVES

II. AIM OF THE STUDY

1. To study the fasting and post prandial lipid levels in patients with type 2 diabetes mellitus

2. To assess the significance of post prandial dyslipidemia with respect to fasting dyslipidemia as cardiovascular risk factor in these patients.

BACKGROUND

III. **BACKGROUND**

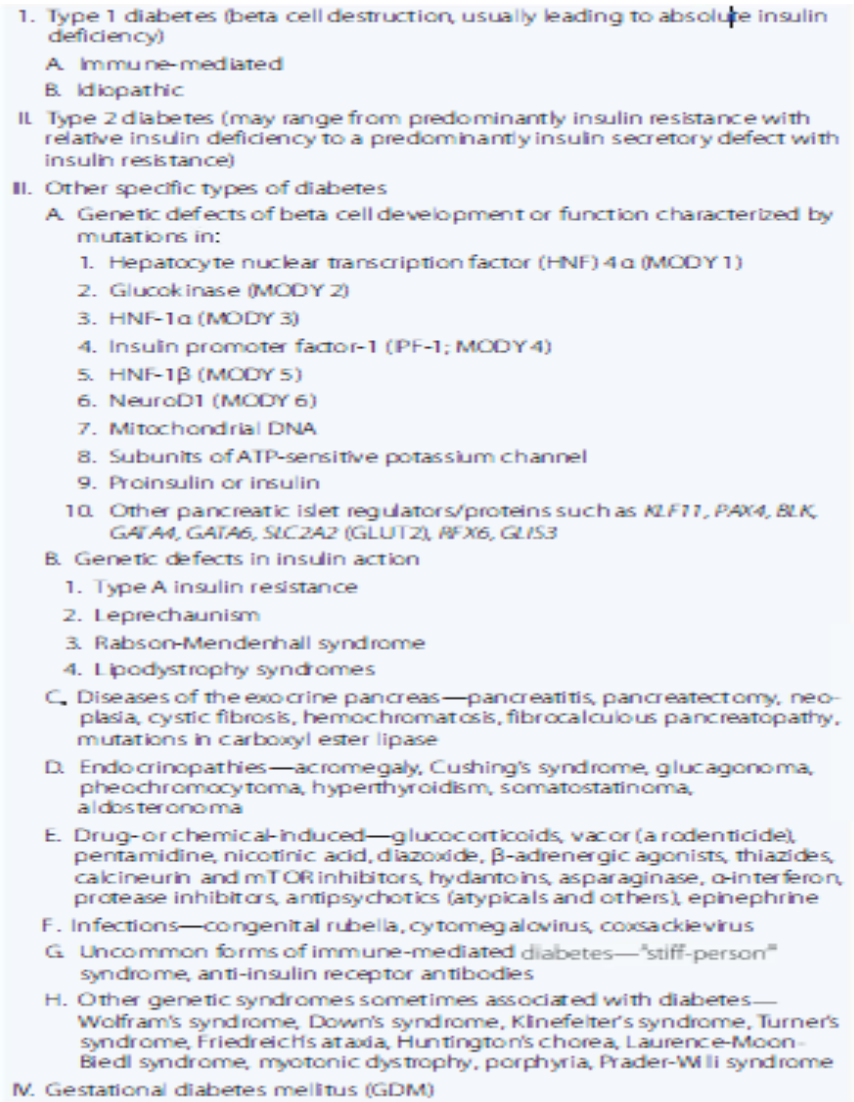
DIABETES MELLITUS

Diabetes mellitus is a chronic disorder characterized by abnormalities metabolism of the fuels of the body , which include glucose, lipids, and amino acids. However, impairment in glucose tolerance are central in both the pathogenesis ,diagnosis and also the classic complications of diabetes. People with diabetes are more prone to develop atherosis because of the abnormalities in lipid metabolism which is associated with diabetes, especially those with type 2 diabetes.

Type 2 diabetes is characterized by both a defect in insulin action (insulin resistance) and a relative insulin deficiency. Insulin resistance generally precedes insulin deficiency by several years in most models of type2 diabetes although recent reports have suggested that a beta-cell defect may be the initiating trigger for both. Elevated levels of fasting or postglucose load insulin levels are the hallmark of insulin resistance.

ETIOLOGICAL CLASSIFICATION

The etiologic classification of diabetes mellitus currently recommended by World Health Organisation and the American Diabetes Association is as follows.



I. Type 1 diabetes (beta cell destruction, usually leading to absolute insulin deficiency)
   A. Immune-mediated
   B. Idiopathic
II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly insulin secretory defect with insulin resistance)
III. Other specific types of diabetes
   A. Genetic defects of beta cell development or function characterized by mutations in:
      1. Hepatocyte nuclear transcription factor (HNF) 4α (MODY 1)
      2. Glucokinase (MODY 2)
      3. HNF-1α (MODY 3)
      4. Insulin promoter factor-1 (PF-1; MODY 4)
      5. HNF-1β (MODY 5)
      6. NeuroD1 (MODY 6)
      7. Mitochondrial DNA
      8. Subunits of ATP-sensitive potassium channel
      9. Proinsulin or insulin
      10. Other pancreatic islet regulators/proteins such as *KLF11, PAX4, BLK, GATA4, GATA6, SLC2A2* (GLUT2), *RFX6, GLIS3*
   B. Genetic defects in insulin action
      1. Type A insulin resistance
      2. Leprechaunism
      3. Rabson-Mendenhall syndrome
      4. Lipodystrophy syndromes
   C. Diseases of the exocrine pancreas—pancreatitis, pancreatectomy, neoplasia, cystic fibrosis, hemochromatosis, fibrocalculous pancreatopathy, mutations in carboxyl ester lipase
   D. Endocrinopathies—acromegaly, Cushing's syndrome, glucagonoma, pheochromocytoma, hyperthyroidism, somatostatinoma, aldosteronoma
   E. Drug- or chemical-induced—glucocorticoids, vacor (a rodenticide), pentamidine, nicotinic acid, diazoxide, β-adrenergic agonists, thiazides, calcineurin and mTOR inhibitors, hydantoins, asparaginase, α-interferon, protease inhibitors, antipsychotics (atypicals and others), epinephrine
   F. Infections—congenital rubella, cytomegalovirus, coxsackievirus
   G. Uncommon forms of immune-mediated diabetes—"stiff-person" syndrome, anti-insulin receptor antibodies
   H. Other genetic syndromes sometimes associated with diabetes—Wolfram's syndrome, Down's syndrome, Klinefelter's syndrome, Turner's syndrome, Friedreich's ataxia, Huntington's chorea, Laurence-Moon-Biedl syndrome, myotonic dystrophy, porphyria, Prader-Willi syndrome
IV. Gestational diabetes mellitus (GDM)

Figure 1 Etiological classification of Diabetes mellitus

TYPE 2 DIABETES MELLITUS

“Type 2 diabetes mellitus which is described as the most prevalent diabetesformis characterized by disorders of insulin action and insulin secretion.

Resistance to insulin is the basis of type 2 diabetes and there is a deficiency of insulin which is relative rather than absolute.The time when the disease is diagnosed, the diabetes patients may not require exogenous insulin treatment to live.Butultimately they require insulin for their glycemic control.”

“Most of these patients are almost obese at the time of development of diabetes, and this obesity increases the insulin resistance. They generally remain undiagnosed for a long period, usually in first few years, because the development of hyperglycemia is gradual and in the earlier stages it may not be severe enough toproduce the classical symptoms of the disease; however, these patients are at increased risk of developing microvascular and macrovascular complications.”

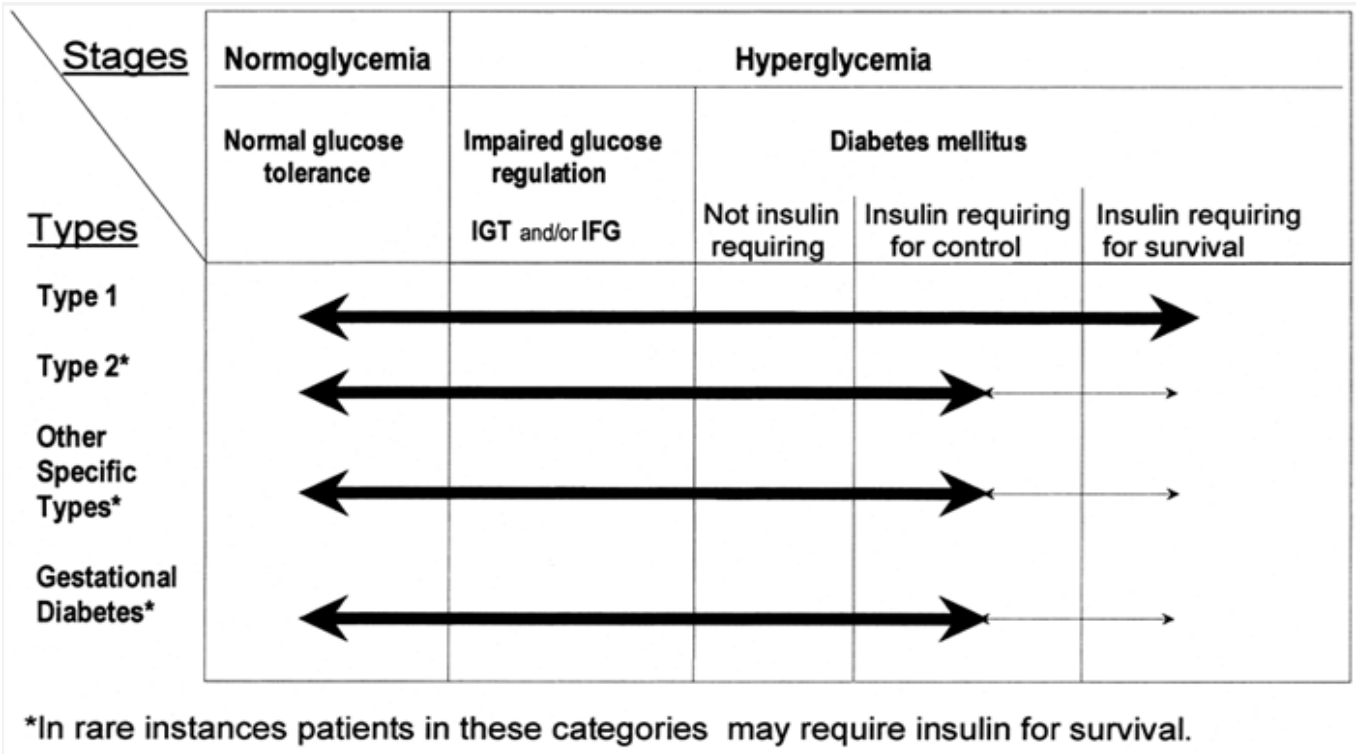


Figure 2 Clinical stages and etiologic types of diabetes.

"The insulin levels in their circulation may be normal or even increased but not amounting to control blood sugar levels within the normal level. This is because of the insulin resistance . Thus, these patients have insulin deficiency which is not absolute but relative. Weight reduction and pharmacologic treatment may reduce this resistance and help in normalising the blood sugar."

"The risk of getting type 2 diabetes mellitus increases as the age, body mass index and physical inactivity increase.Type2 diabetes shows strong familial aggregation, so that persons with a

positive family history of disease in the sibling or parent are at more risk of getting the disease. The incidence also increases in individuals with dyslipidemia, hypertension or obesity and females with a past history of GDM.”

“Most patients with T2DM exhibit two apparently different defects: (a) insulin resistance- an impairment in the ability of muscle and fat to respond to insulin by increase in glucose uptake and of liver to respond with decreased glucose output; and (b) failure of β-cell to secrete large amount of insulin to compensate for this insulin resistance .”

DIABETIC DYSLIPIDEMIA

"The term *insulin resistance* refers to resistance to the metabolic effects of insulin, including the suppressive effects of insulin on endogenous glucose production, on adipose tissue lipolysis and the stimulatory effects of insulin on glycogen synthesis and peripheral (predominantly skeletal muscle) glucose uptake."

"MI, CVA, and other cardiovascular disease are the cause of death in up to 80% of patients with T2DM. Independent of other risk factors, Diabetes increases the risk of cardiovascular morbidity and mortality but also has a compounding interaction with factors such as smoking, hypertension, and dyslipidemia.

The risk factor that is overriding for coronary artery disease in insulin resistance and T2DM is diabetic dyslipidemia,the profile of which includes hypertriglyceridemia, low HDL, and high small, dense LDL particle concentrations. The percentage of men with T2DM who have abnormal cholesterol levels is not different from that of nondiabetic men with abnormal cholesterol. However, diabetic women have nearly double the rate of hypercholesterolemia.The physiologic basis for this abnormal lipid profile appears to be overproduction of apolipoprotein B–containing VLDL particles. The apolipoprotein B production by the liver is primarily post-translational and augmented by insulin and by the increased availability of FFAs

in the portal circulation, probably as a result of increased lipolysis in the visceral adipose tissue."

" There is overproduction of VLDL triglyceride which results in the increase in the transfer of VLDL triglyceride to HDL particles in exchange for HDL cholesterol esters mediated by the cholesterol ester transfer protein.The triglyceride-rich HDL is hydrolyzed to small HDL by hepatic lipase, which is metabolised readily by the kidneys, which results in low HDL in serum. CETP–mediated exchange of VLDL triglyceride for LDL and subsequent triglyceride hydrolysis by hepatic lipase result in generation of the small and dense LDL particles found in insulin-resistant people".

"The increased risk in heart disease in diabetic patients has prompted to recommend that diabetic patients be treated for dyslipidemia as aggressively as patients with history of MI."

ADVANCED GLYCATION END PRODUCTS IN DIABETES

"AGEs occur as a result of the nonenzymaticglycation of both lipids and proteins. Initially, a labile covalent bond develops between the aldehyde of the glucose molecule and the amino acid side chain on both sugars and lipids. Specifically, glucose is covalently bound mainly to lysine residues in proteins, forming fructose-lysine residues. This reaction results in the development of a Schiff base, which, in turn, undergoes another chemical reaction to form a ketoamine, termed an Amadori product. These products result in cumulative

oxidative damage to proteins. These products include CML and pentosidine. The increased levels of pentosidine and CML correlate with the severity of diabetic complications, including nephropathy, retinopathy, and vascular disease. One such Amadori product is glycated (or glycosylated) hemoglobin A_{1c}(HbA_{1c}), which is commonly used to monitor glycemic control in diabetic patients. Since both free-radical oxidation and glycation are involved, these substances are also called glyoxidation products."

"AGEs cross-link to the proteins composing the extracellular matrix and vascular basement membrane, which results in reduced solubility and decreased enzymatic digestion . AGE formation also prevents proper assembly of basement proteins, thereby altering their function. This in turn may alter the ability of cells to bind to their substrates."

"AGEs are derived from oxidation of lipids . The side chains of unsaturated fatty acids undergo oxidation, which yields reactive carbonyl-containing fragments [malondialdehyde (MDA), glyoal 4-hydroxynonenal (4-HNE)] and then react with amino groups, mainly lysine residues."

"Enhanced glycation, oxidation, and glyoxidation of lipoproteins have been postulated as a possible cause for the development of diabetic macrovascular disease. Certainly there are increased levels of AGE-modified LDL-apoprotein and LDL-lipid in persons with diabetes relative to levels in persons without diabetes . This would suggest that even in the face of similar glycemic control and other cardiovascular risk factors, the development of diabetic vascular complications would depend on differences of oxidative stress as well as on the tissue level of antioxidants."

“The evidence for this possible role of these altered lipoproteins includes the presence of oxidized lipoproteins in the vessel wall and the demonstration of lesion regression with antioxidants . One study showed that the susceptibility of LDL to oxidation was correlated with the degree of atherosclerosis in 35 male survivors of an MI.”

“Vlassara and colleagues identified a specific receptor for AGEs on monocyte/macrophages, termed RAGE (receptor for AGEs). The subsequent interaction with the AGE and its receptor may induce the release of the cytokines tumor necrosis factor (TNF) and interleukin-1 . Other cytokines that have been demonstrated include the synthesis and release of procoagulant activity and platelet-activating factor (PAF) by endothelial cells , as well as the induction of platelet-derived growth factor (PDGF-AA), which can be indirectly responsible for fibroblast and smooth muscle proliferation . Furthermore, increased AGE-receptor interaction has been shown to result in the enhanced expression of vascular cell adhesion molecule (VCAM) , which in turn results in increased atherogenesis.”

“The important role of the AGE receptor in the development of atherosclerosis was further strengthened by the demonstration that atherosclerosis was less severe in the usually atherosclerotic apolipoprotein E-knockout mice when they were administered an antibody-fragment that neutralized RAGE . This effect was seen without any effect on glycemic control or lipoprotein profile.”

“Several factors involved in clotting , including fibrinogen, factor VII, and plasminogen activator inhibitor 1 (PAI-1), have been shown to be increased in insulin resistance.Insulin increased expression of PAI-1 in hepatocytes, endothelial cells,

and abdominal adipose tissue, and insulin-sensitizing drugs decreased PAI-1 activity."

"Obesity involving the upper part of the body rather than lower-body (the apple rather than the pear shape) is highly correlated to insulin resistance . Thus, the distribute of the fat in the body , rather than the degree of obesity, appears to determine the cardiovascular risk .The reported association between increased abdominal (upper-body) fat and an increased risk of coronary heart disease is related to visceral fat, for which the waist-to-hip ratio is a convenient index. A waist-to-hip ratio greater than 1.0 in men and greater than 0.8 in women indicates abdominal obesity."

"Waist circumference is measured at the midpoint of the lower margin of the Lowest palpable rib and the top of the iliac crest, using a stretch-resistant tape that provides a constant 100 g tension. Hip circumference is measured at the widest portion of the buttocks, with the tape parallel to the floor. For both measurements, the subject should stand with feet close together, arms at the side and body weight evenly distributed, and should wear little clothing. The subject should be relaxed. The measurements are to be taken at the end of a normal expiration. Each measurement should be repeated twice; if the measurements are within 1 cm of oneanother, the average should be calculated. , the two measurements should be repeated ,If the difference between the two measurements exceeds 1 cm."

MEASURES OF OBESITY AND ABDOMINAL OBESITY AND CARDIOVASCULARDISEASE RISK

"Based on extensive review, concluded that there was convincing evidence that measures of general obesity (e.g. BMI) and measures of abdominal adiposity (e.g. waist circumference, waist–hip ratio and waist–height ratio) are associated with CVD risk factors and incident CVD events. It was also concluded that measures of abdominal obesity are better than BMI as predictors of CVD risk, although combining with BMI discriminatory capability was more ."

" The pathogenesis of the components of metabolic syndrome iscomplex and not well understood, central obesity , insulin resistance are Proposed as important causative factors.

Abdominal obesity, easily assessed using waist circumference and WHR independently associated with metabolic syndrome components including insulin resistance."

"AtherogenicdyslipidaemiaIS the combination of increased triglycerides (TG) and low concentrations of HDL-c together withelevated small dense LDL and small HDL particles, all of which are independently atherogenic."

"Adipose tissue is classically viewed as simply the site for storage of excess energy in the form of triglycerides. However, it is now clear that adipose tissue secretes a variety of endocrine and paracrine factors that have significant effects on metabolism.Theseadipokines regulate a diverse array of actions, including alterations in feeding behavior; changes in liver, muscle, and adipose tissue insulin sensitivity; vascular reactivity; and atherosclerosis progression."

LEPTIN

"Leptin is a protein synthesized mainly in adipose tissue. Leptin suppresses feeding behavior, and humans with mutations in leptin are morbidly obese and insulin resistant. However, studies from a number of laboratories, indicate a direct role for leptin in lipid metabolism, including increased metabolic rate, lipolysis, stimulation of fatty acid oxidation, inhibition of lipogenesis, and increases in AMPK activity. In obesity there is leptin resistance"

ADIPONECTIN

"Adiponectin is a 30-kd protein synthesized and secreted from adipocytes The HMW form may be further cleaved to forms that may be the active transducer of signaling. Disruption of adiponectin predisposes them to high-fat diet–induced insulin resistance. Adiponectin levels are low in humans with obesity and insulin resistance and are increased by insulin-sensitizing PPARg agonists.

RESISTIN

Resistin is a protein that is synthesized and secreted from adipocytes.Resistin levels are elevated in both diet-induced obesity."

TUMOR NECROSIS FACTOR-A

"TNF-α is a transmembraneprotein.Elaborated by multiple tissues,. It has primarily a paracrine effect which leads to induction of insulin resistance . Systemic

effects of TNF-α include insulin resistance in skeletal muscle and the induction of lipogenesis in the liver"

MONOCYTE CHEMOTACTIC PROTEIN-1

"Monocyte chemotatic protein-1 (MCP-1) is increased in proportion to adipose tissue mass and correlates with insulin resistances."

INTERLEUKIN-6

"IL-6 is a glycoprotein that circulates at relatively high concentrations proportionately to the degree of adiposity. People with increased level of IL-6 have shown to have increased insulin resistance, hepatic glucose production, lipolysis, and fatty acid oxidation. About a third of circulating IL-6 is secreted by adipocytes."

LIPID BIOCHEMISTRY AND CHOLESTEROL METABOLISM

"Lipids are complex hydrophobic molecules which are minimally or insoluble in water. They maintain cellular integrity and also allow compartmentalization in the cytoplasm into specific organelles. The major functions of lipids are

-in the form of stored nutrients (triglycerides),

-as precursors of adrenal and gonadal steroids and bile acids (cholesterol)

-as intracellular and extracellular messengers (e.g., prostaglandins, phosphatidylinositol).Lipoproteins provide a vehicle for delivering lipids to cells

throughout the body and transporting the complex lipids as water-soluble complexes in the blood."

CLASSES OF LIPIDS. STRUCTURE AND FUNCTION

FATTY ACIDS

"Fatty acids vary in the number and position of double bonds and the length. Saturated fatty acids lack double bonds and unsaturated fatty acids have one or more double bonds. MUFA have one double bond, and polyunsaturated fatty acids (PUFAs) have two or more."

CHOLESTEROL

"Cholesterol is a hydrocarbon with an eight-carbon side chain and four-ring. It plays a major role as a precursor of steroid hormones (adrenal and gonadal hormones) and as a component of cell membranes. Cholesterol is also a precursor of bile acids formed in the liver, stored in the gallbladder, and secreted in the intestine for the absorption of fat. In the blood, about two thirds of the cholesterol is esterified."

SYNTHESIS OF CHOLESTEROL

"Three molecules of acetate are condensed to form 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA), the enzyme HMG-CoA reductaseconvertes to mevalonic acid. Mevalonic acid through a series of steps,is converted to cholesterol. The rate-limitingstep in cholesterol biosynthesis is HMG-CoA reductase. The statins which are the Competitive inhibitors of this enzyme reduce cholesterol biosynthesis ."

METABOLISM OF DIETARY LIPIDS

"The digestion of dietary fats occurs starting from the stomach and continues in the small intestine(proximal). Triglycerides are hydrolyzed to FFAs and mono- and diglycerides, cholesteryl esters are hydrolyzed to free cholesterol, and phospholipids are converted primarily to lysolecithin. Bile salt micelles disperse and partially solubilize water-insoluble lipids; this facilitates the intestinal transport and delivery of lipids to the unstirred water layer of intestinal epithelial cells, where they can be taken up by the cells. Bile acids also activate pancreatic lipase, which participates in the hydrolysis of triglycerides. Long-chain fatty acids (LCFA) are taken up by the enterocytes in the duodenum and proximal jejunum, re-esterified into triglycerides, and used in the biosynthesis of intestinal lipoproteins (chylomicrons), which are delivered to the mesenteric lymph and enter the general circulation with the thoracic duct lymph. Bile acids are reabsorbed from the ileum, enter the portal blood after which they are taken up by the liver."

TRIGLYCERIDE AND FREE FATTY ACID METABOLISM

STORAGE AND USE

"Free fatty acids are released from triglycerides of chylomicrons and very-low-density lipoproteins (VLDLs) through the action of lipoprotein lipase (LPL) which is bound to the capillary endothelial cells in the adipose, muscle, and breast tissue, where it liberates FFAs."

In adipose tissue, high levels of glucose and insulin promote the conversion of FFAs to triglyceride for storage. Insulin stimulates LPL activity and fatty acid esterification through the formation of glycerol phosphate and decreases FFA release through the inhibition of hormone-sensitive lipase. In diabetes mellitus,which has a impaired insulin action is associated with decreased LPL activity. Insulin and glucose also stimulate the biosynthesis of FFAs in the liver and, to a lesser degree, in adipocytes when dietary fat is replaced by carbohydrate.

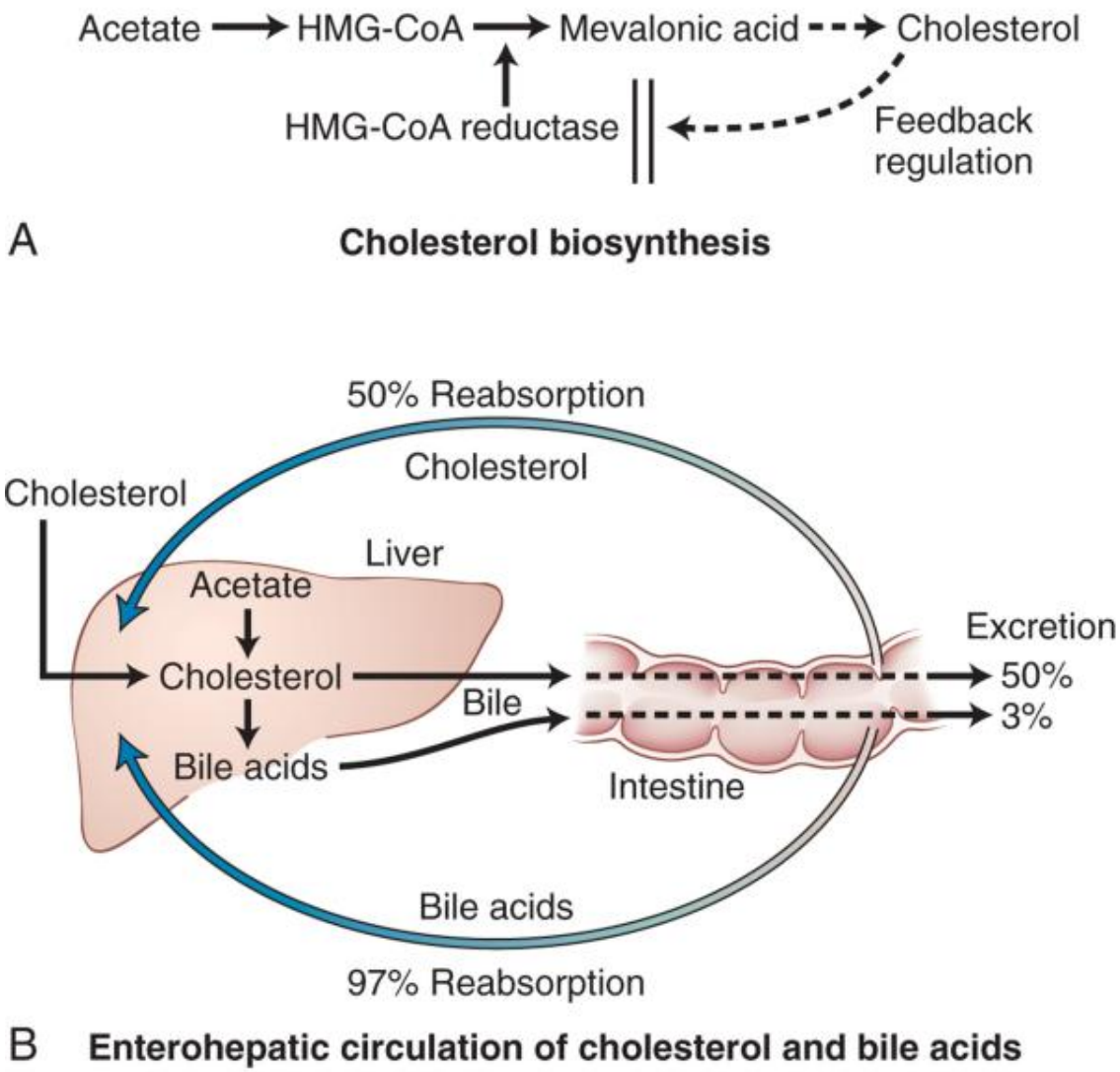


Figure 3.Cholesterol biosynthesis and entero-hepatic circulation

FATTY ACID RELEASE FROM ADIPOSE TISSUE

The net release of FFAs and glycerol occurs during including stress, exercise, fasting, and uncontrolled diabetes mellitus. Unlike many hormones, insulin inhibits rather than stimulates hormone-sensitive lipase in adipose tissue. **Figure4**

HORMONES THAT AFFECT LIPOLYSIS IN VITRO

RAPID STIMULATION
Catecholamines (β-1 agonists)
Corticotropin
Glucagon
Placental lactogen
Prolactin
Secretin
Thyrotropin
Vasoactive intestinal peptide
Vasopressin
SLOW STIMULATION
Glucocorticoids
Growth hormone
SUPPRESSION
Gastric inhibitory polypeptide

Insulin
Oxytocin
Prostaglandin
Somatomedins

FATTY ACID BIOSYNTHESIS

Normally fatty acids are supplied by diet. Longer fatty acids, such as stearic acid or oleic acid , are synthesized from palmitic acid .In this way, fatty acid synthesis can meet most of the body's requirements

Essential PUFAs cannot be synthesized but must be supplied in the diet. These are linoleic acid and linolenic acid. Essential fatty acids are required for a prostaglandin synthesis.

PLASMA LIPOPROTEINS

GENERAL STRUCTURE AND MAJOR CLASSES OF LIPOPROTEINS

Lipoproteins are the vehicles for the transport of lipids as soluble complexes of lipids and proteins. The lipids are triglycerides, cholesteryl esters, free cholesterol, and phospholipids. The protein moieties are called apolipoproteins. Lipoproteins also transport vitamins A, D, and E, drugs (e.g., probucol, cyclosporine), some viruses,

and some antioxidant enzymes (e.g., paraoxonase and platelet-derived activating factor hydrolase.)

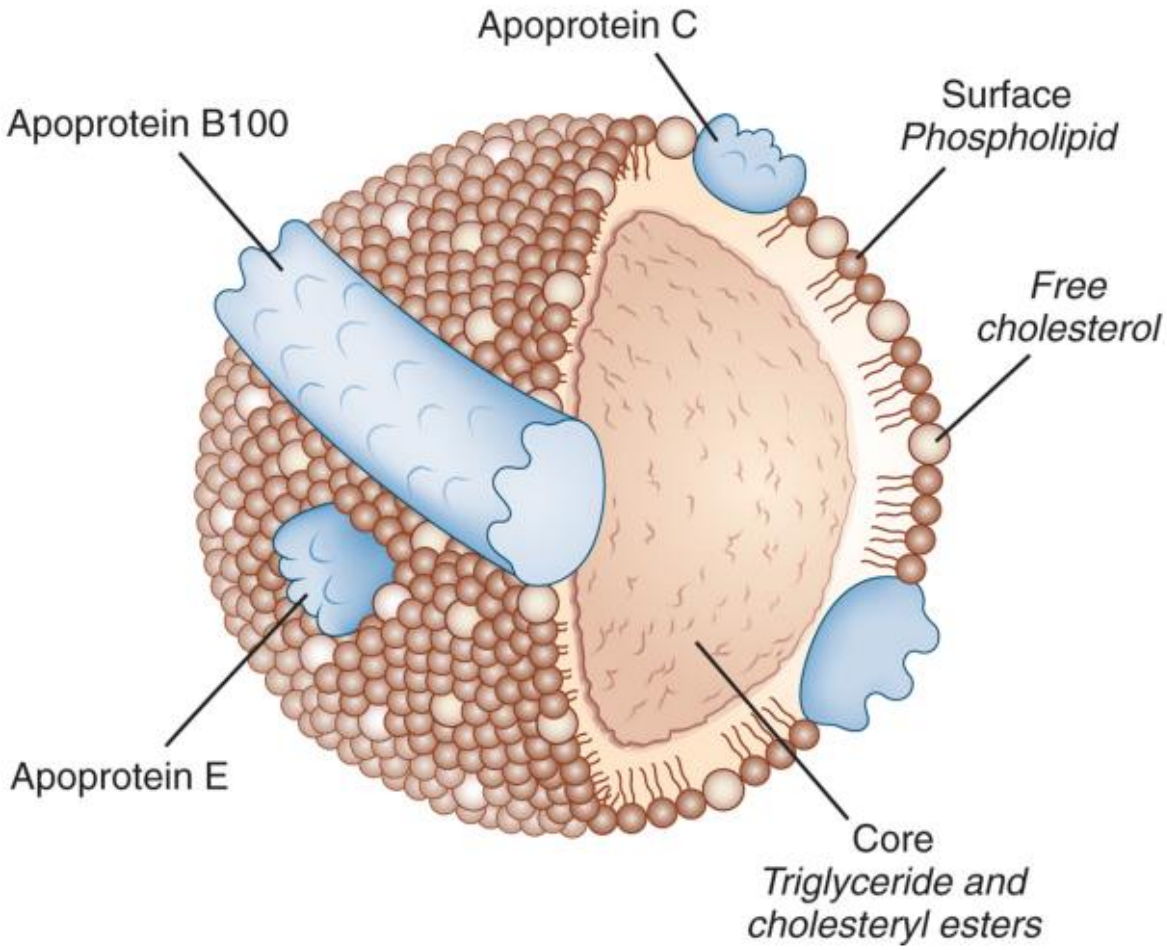


Figure4 –Structure of Lipoprotein

Lipoproteins are spherical structures with a core formed ofhydrophobic lipids (triglycerides and cholesteryl esters) and a surface formed of layer ofhydrophilic

constituents, namely protein, free cholesterol, and phospholipids .differentlipoproteins play different roles in lipid transport and the apolipoproteins on the surface determine their fate .

CHYLOMICRONS

CHARACTERISTICS

Chylomicrons are the largest of the plasma lipoproteinscomposed of 98% to 99% lipid (85%-90% triglyceride) and 1% to 2% protein and readily float after ultracentrifugation of plasma. Chylomicrons are present in postprandial plasma .The distinctive apolipoprotein is apo-B48, a form of apo-B that has an apparent molecular mass 48% that of apo-B100. Because it is the only form of apo-B synthesized by the intestine, apo-B48 is a marker for human lipoproteins produced by the intestinal epithelium.

ORIGIN

Chylomicrons are produced by the epithelial cells of the small intestine.Triglycerides, phospholipids, and cholesterol are used for chylomicron formation in the Golgi apparatus. From there, through mesenteric lymph, the thoracic duct lymph to enter the general circulation.

Intestinal cholesterol absorption which appears to be the target for ezetimibe, which inhibits intestinal cholesterol absorption. . After their synthesis in the ER, the triglycerides are transferred to apo-B48 for assembly of the particles.

METABOLIC FATE

In the circulation, LPL catalyzes chylomicron triglycerides to release FFA and converts them into triglyceride-poor, cholesterol-enriched chylomicron remnants .rapid clearance of Chylomicron remnants is done by the liver. .

VERY-LOW-DENSITY LIPOPROTEINS

CHARACTERISTICS

VLDLs are composed of 85% to 90% lipid (about 55% triglyceride, 20% cholesterol, and 15% phospholipid) and 10% to 15% protein. They are formed of apo-B100, the hepatic form

ORIGIN

VLDLs are synthesized by the liver when increased FFAdelivery to the hepatocytes, either by high dietary fat or by mobilization of fatty acids from adipose tissue with fasting or uncontrolled diabetes mellitus.

METABOLIC FATE

By the actions of LPL and hepatic lipase VLDL triglycerides are hydrolyzedintoremaning IDLswhicg retain apo-B100 and apo-E. Approximately half

of VLDLs become LDLs, and the remainder cleared directly by the liver as VLDL remnants .The IDLs are precursors of LDLs andareVLDL which are atherogenic.

LOW-DENSITY LIPOPROTEINS

CHARACTERISTICS

LDLs , the major cholesterol-carrying lipoproteins; are composed of approximately 75% lipid (about 35% cholesteryl ester, 10% free cholesterol, 10% triglyceride, and 20% phospholipid) and 25% protein.The principal protein are Apo-B100, along with trace amounts of apo-E .

ORIGIN

VLDLs undergo lipase-mediated hydrolysis to form LDLs . The surface lipids and proteins are remodeled as the the triglyceride-rich core is removed from VLDLsn and excess surface constituents are transferred to HDL, which forms small, cholesterol-rich LDL.

METABOLIC FATE

hepatocytes take up About 75% of LDL . LDLs are considered to be atherogenic.

FACTORS AFFECTING LOW-DENSITY LIPOPROTEIN LEVELS IN THE BLOOD

Plasma LDLc can be increased through increased VLDL biosynthesis and secretion caused by increased flux of FFAs to the liver from dietary fats or from adipose tissue, and the other is decreased LDL catabolism.

High-Density Lipoproteins

CHARACTERISTICS

HDLs are small particles containing about 50% lipid (25% phospholipid, 15% cholesteryl ester, 5% free cholesterol, and 5% triglyceride) and 50% protein .

ORIGIN

HDLs originate from three major sources ,first being the liver secreting an apo-AI-phospholipid disc called nascent or precursor HDL (pre-β HDL).,Second being the intestine synthesizing a small apo-AI–containing HDL particle and third being those from surface material (primarily apo-AI and phospholipid) that comes from chylomicrons and VLDLs during lipolysis.

HIGH-DENSITY LIPOPROTEINS AS ANTIATHEROGENIC LIPOPROTEINS

“People with high levels of HDL-C have lower incidence of CHD due to its role in reverse cholesterol transport,leading to redistribution of cholesterol away from

the artery wall.they have inhibitory action on monocyte adhesion and antioxidative activity that could prevent LDL oxidation. paraoxonase and PAF-AH present in HDL possess antioxidative activity."

LIPIDS AND ATHEROSCLEROSIS

CHOLESTEROL AND CARDIOVASCULAR DISEASE

"Even in the presence of other risk factors total cholesterol levels of less than 160 mg/dL markedly decrease CHD risk,. Major conditions dyslipidemia, hypertension, cigarette smoking, and diabetes account for increased CHD risk in 90% of patients."

"LDL-C levels are a strong predictor of CHD and atherosclerosis, it was expected that LDL would be taken up avidly by macrophages, leading to the formation of foam cells."

"The physiologically important LDL modification probably involves oxidation and results in lipid peroxidation which participate directly in atherogenesis by serving as chemoattractants for circulating monocyte-macrophages"

OVERVIEW OF ATHEROGENESIS

"Atherogenesis is the process that ultimately leads to impaired blood flow to the heart, brain, and other organs, causing ischemia or infarction. Response to injury,

process by which endothelial cell dysfunction occurs in response to various injuries to the artery wall and initiate lesion formation. Cholesterol-rich atherogeniclipoproteins injures the endothelium contributing to the lipid accumulation in the intima of the artery."

"The lipid-laden foam cells and lymphocytes and produce various inflammatory molecules and proteolytic enzymes that alter the nature of the lesion. Antigens, eg.oxidized LDL, are presented by macrophages to the type 1 helper T (Th1) cells which initiate the production of inflammatory and cytotoxic molecules from macrophages. The cytokines interleukin-6 , stimulates the production of acute-phase reactants, such as C-reactive protein (CRP)"

"There is a compensatory expansion of the lumen as atherosclerosis progresses. The exposure of the lesion content to platelets and initiates thrombosis when rupture of the overlying intima or endothelial erosion takes place which occurs mainly in the place where the fibrous cap is thin. It is the acute thrombosis, not arterial lumen stenosis, that is responsible for infarctions."

STEPS IN ATHEROSCLEROTIC LESION FORMATION

"Initial events is the focal attachment of circulating monocytes to the endothelial surface . Oxidized or modified LDLs are retained in the subendothelium is the major initiating factor for the adherence of monocytes. The monocytes modify the endothelial surface and induce adherance, enter the subendothelial space, and differentiate into macrophages where they become entrapped in the matrix and

undergo oxidation.the macrophages engulfing theoxidized LDL leads to formation of foam cells The first grossly visible atherosclerotic lesion is referred to as a fatty streak The recruitment of monocytes continues, and smooth muscle cells begin to migrate into the intimaAs the cycle of interactions continues, a proliferative or fibrous plaque is formed. The foam cells begin to necrose,and cholesterol crystals develop. The death of foam cells leads to extracellular lipid deposition, accompanied by collagen synthesis and smooth muscle cell migration and proliferation.progresses to the complicated lesion stage .”

“The surfaces of complicated lesions can become thrombogenic as endothelial cells are lost or the fibrous cap ruptures and the subendothelial space is exposed. Platelets can adhere to this exposed surface, promoting thrombus formation.Calcification is a feature of late lesions. Advanced lesions can weaken the elasticity and integrity of the artery wall, with the potential to lead to an aneurysm of the vessel.”

HYPERLIPIDEMIA AND DYSLIPIDEMIA. DEFINITIONS AND OVERVIEW

“The guidelines suggest Total cholesterol between 170 and 200 mg/dL is borderline high and levels greater than 200 mg/dL are high. For triglycerides, the cutpoint is150 mg/dL.These boundaries are arbitrary,The prevalence of CHD events in those with desirable cholesterol levels 150-200 mg/dL is actually 20 out of 100 persons. Patients with desirable total cholesterol levels who develop CHD commonly have low HDL-C levels and high triglyceride values. “

“Hyperlipidemia is caused by increased concentrations of plasma lipoproteins classified as primary genetic disorders or secondary disorders”

“Diabetes mellitus exerts profound effects on plasma lipid metabolism, upto one third of all diabetic patients have Hypertriglyceridemia related to the role of insulin in the production and clearance of triglyceride-rich lipoproteins from the plasma, In addition, , predisposing diabetic patients to premature CHD, a leading cause of death in diabetes is the high plasma levels of atherogenic lipoproteins and low HDL”

“This chronic hyperglycaemia of diabetes is associated with a long term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and the blood vessels. The risk of the chronic complications increases as a function of the duration of the hyperglycaemia. Since Type 2 DM, often, has a long asymptomatic.”

“Period of hyperglycaemia, many individuals with Type 2 DM have complications at the time of their diagnosis. The macrovascular complications such as coronary heart disease and cerebrovascular disease are two to four times greater in the patients with Type 2 DM. Other factors(dyslipidemia and hypertension) also play important roles in the macrovascularcomplications. The postprandial dysmetabolism and the associated oxidative stress may link the insulin resistance and the Type 2 DM to the disproportional incidence of cardiovascular disease.”

“In type 2 diabetes, (more than 90% of cases), the metabolic defect is insulin resistance and relative insulin deficiency which iscaused by both genetic and acquired

factors including the insulin resistance, obesity, hyperglycemia, hypertension, plasma lipid abnormalities, and hyperuricemia, which are referred to as syndrome X or the metabolic syndrome ,the most common lipid abnormalities in type 2 diabetes is a moderate hyperlipidemia with VLDL, chylomicronemia, depending on how well blood glucose levels are regulated and on the dietary fat intake The fasting triglyceride and cholesterol levels are often moderately elevated, the HDL-C is usually low, and remnants of VLDL and chylomicrons, which are atherogenic, are increased. Plasma levels of LDL are increased in some. the hyperlipidemia in type 2 diabetes is often characterized by an increase in small, dense LDLs which are particularly atherogenic."

" The lipoprotein abnormalities in type 2 diabetesis due to decreased LPL activity in muscle and adipose tissue .There is increased FFA flux to the liver from adipose tissue stores. Insulin resistance leads to combined hepatic overproduction of apo-B and the,the FFA flux which drives triglyceride synthesis and VLDL production in the liver."

"Glycemic control by regular exercise, diet, oral hypoglycemic drugs, or insulin therapy is the cornerstone of therapy for diabetic dyslipidemia. Decreasing insulin resistance through weight loss and exercise can, however, have dramatic effects on both the hyperglycemia and the hyperlipidemia. Metformin, may lower plasma glucose levels and produce a modest lowering of plasma lipid levels. drugs for diabetic hyperlipidemia include HMG-CoA reductase inhibitors, a mandated therapy for all T2DM patients and, in certain cases, addition of fibrate or niacin

therapyisbeneficial. Niacin can impair or worsen glucose tolerance so should be used with caution. Treatment with insulin can lower plasma LDL-C .”

POSTPRANDIAL LIPEMIA AS A RISK FACTOR FOR DEVELOPMENT OF CVD

“Postprandial lipemia is increased lipoprotein and chylomicron in acute response to a high-lipids meal whichover time return to baseline levels. a new perspective is openedin Postprandial lipemia measurement for studies that is aim to compare intervention methodologies for treatment”

“Atherogenesis is closely associated with postprandialhyperlipemia, since experiments with animals and humans have shown that endothelial cells can pick up chylomicron remnants and LDL-c. Clinical studies have shown that the magnitude of postprandial lipemia or even elevated levels of postprandial TAG can predict symptomatic or asymptomatic atherosclerosis, independently of fasting analysis.”

“Epidemiologic studies, clinical trials and current scientific literature show that increasing PL is directly linked to the progression of atherosclerotic plaques, either through deposition of lipoprotein debris on the arterial surface or in an indirect manner with predominance of lipoproteins such as chylomicrons, VLDL and LDL.”

“Postprandial lipemia is characterized by a state of hypertriglyceridemic transition and reflects an integrated measure of individual ability to remove TAG, the fasting concentrations of which, in turn, have been shown to be related to the size of LDL-c particles. This response can be subject to increased fatty acid mobilization, synthesis of VLDL-c and delays in its removal, providing greater interaction between

lipoproteins and contributing to the formation of small dense particles of LDL-c, which are highly atherogenic. Therefore, interventions to attenuate postprandial lipid response can be considered beneficial to cardiovascular health.”

“Consumption of food by human beings is evenly distributed throughout the day . By definition, the fasting state is after an 8-hour fastthus, for the majority of a 24-hour period, humans find themselves in the nonfasting state with the exception of the early morning hours. Recent study showed that nonfasting triglycerides were better than fasting triglycerides at predicting cardiovascular events. As atherogenesis may be a postprandial phenomenon, future research should focus on studies reducing the levels of nonfasting triglycerides and thus remnant lipoprotein cholesterol in an attempt to reduce the risk of cardiovascular disease and .and also using nonfasting rather than fasting lipid profiles for cardiovascular risk prediction would simplify clinical care for patients worldwide. Nonfasting levels predict cardiovascular events, our data challenge the necessity for asking patients to fast before measurement of lipid profiles for cardiovascular risk prediction.”

“With increased availability of palatable food, people tend to overconsume and thusincrease caloric intake well in excess of caloric expenditure . Palatability of foods may bealtered through an alteration of fat and sugar content.This naturalattactiveness Towardsweetness is responsible for a substantial comsumption of sugars . These sugars may occurnatually or can be manufactured and include sucrose, fructose and glucose. Themonosaccharides glucose and fructose are present in small amounts in fruits and honey .”

“Sucrose, a disaccharide formed by one molecule of fructose and one molecule of glucose bondedtogether with an α 1-4 glycoside bond, is found in sugar cane and beets. Fructose can also befound in high fructose corn syrup (HFCS) which consist of a combination of fructose andglucose,”

“Processed food because its adds sweetness, being 100% sweeter than sucrose, enhances color andtexture, perserves the food, is a cheaper alternative to sucrose 6 and can improve sportsperformance . HFCS is also a lower glycemic food than glucose, making it seem like abeneficial alternative to glucose for diabetics.”

“Parallel to therise rate of obesity over that same time period . Today, the averageperson consumes 60-70 g/day of HFCS alone ; leading many researchers to believe that a causitive link beween obesity and fructose consumption may exist.”

“There is a growing body of evidence in animal and human models that high dietary intakeof fructose is an important nutritional factor associated with development of insulin resistance fatty liver , elevated uric acid , hyperlipidemia and hypertension and an increase insmall-dense low-densitiy lipoproteins; all risk factors associated with metabolic syndrome.”

ACUTE CORONARY SYNDROMES IN PATIENTS WITH DIABETES

“Acute ischemic events represent a major cause of death in the diabetic population . Diabetic patients who suffer an MI have a higher mortality than nondiabetic patients both in the acute phase and on long-term follow-

up. Numerous studies have shown that in-hospital mortality rates from MI in patients with diabetes are 1.5- to 2-fold higher than in patients without diabetes . Diabetes remains an independent predictor for a poor prognosis in the thrombolytic era. In the Thrombolysis and Angioplasty in Myocardial Infarction (TAMI) trials, the in-hospital mortality rate was nearly twice as high in patients with diabetes, with more congestive heart failure and twice the rate of clinically recognized reinfarction.”

“Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-I) trial, mortality at 30 days was highest among patients with diabetes treated with insulin (12.5%) compared with patients with diabetes not treated with insulin (9.7%) and nondiabetic (6.2%) patients (p <0.001) . Similar results have been reported from the other large studies . Diabetes is also a risk factor for cardiogenic shock in the setting of acute ischemic syndromes . Overall, despite the overall improvement in survival from an acute MI with thrombolysis, the in-hospital mortality rates in patients with diabetes remain 1.5 to 2 times higher than in patients without diabetes .”

“This increased in-hospital mortality among patients with diabetes with acute MI is due predominantly to an increase in the incidence of congestive heart failure , although increases in the incidence of reinfarction, infarct extension, and recurrent ischemia have also been reported .”

“Studies using serial determinations of total creatine kinase activity , radionuclide ventriculography, or echocardiography have found no evidence that patients with diabetes sustain more extensive infarctions than their nondiabetic counterparts . Thus, congestive heart failure and cardiogenic shock are more common and more severe in subjects with diabetes than would be expected from the size of the index infarction . The observation that clinical manifestations of heart failure occur in patients with diabetes despite a modest decrease in left ventricular ejection fraction (EF) led to the suggestion that preexisting diastolic dysfunction is a major culprit in the congestive symptoms . Indeed, subclinical diabetic cardiomyopathy, which is characterized by diastolic dysfunction , is likely to be an important factor in this setting.”

“It should be emphasized, however, that reductions in both left ventricular EF and the regional EF of the noninfarcted myocardium have been well documented in patients with diabetes following MI as compared with patients without diabetes. For example, early angiography in the TAMI trials has demonstrated worse ventricular function in the noninfarcted zone in patients with diabetes .”

“The performance of the left ventricle following MI is determined largely by the extent of coronary disease and the quality of collateral circulation. Thus, the diffuse nature of coronary atherosclerosis in diabetes may contribute to systolic dysfunction of the noninfarcted myocardium. Moreover, a recent study has shown that patients with diabetes have a

reduced ability to develop collateral blood vessels in the presence of CAD , a finding that also may explain the more frequent occurrence of postinfarction angina and infarct extension" .

"Patients with diabetes surviving MI also suffer higher late mortality rates than patients without diabetes . Late mortality is related primarily to both recurrent MI and the development of new congestive heart failure ."

OBESITY MANAGEMENT

"Management of obesity has been shown to delay the progression from prediabetes to type 2 diabetes It may also be beneficial for treating type 2 diabetes.Modest and sustained weight loss has been shown to improve glycemic control and reduce the need for glucose lowering medications"

LIFESTYLE CHANGES FOR OBESITY MANAGEMENT

"Diet, physical activity, and behavior therapy designed to achieve 5% weight loss are recommended for overweight andobese individuals with type 2 diabetes who are motivated to lose weight"

HIGH-INTENSITY INTERVENTIONS

" Focus on diet, physical activity, and behavioral strategies to achieve a 500-750 kcal/day deficit.Recommendations for individuals who achieve short-term weight loss."

“Prescribe a long-term (more than 1 year) comprehensive weight management programMake contact with the patient at least monthly, with ongoing monitoring of body weight thereafter.Prescribe a reduced-calorie dietEncourage high levels of physical activity (200-300 mins/wk).To achieve short-term weight loss, recommend.Short-term (3-month) high-intensity lifestyle interventions that use low-calorie diets (fewer than800 kcal/day) Long-term comprehensive weight management counseling to maintain weight loss.”

PHARMACOLOGIC THERAPY FOR OBESITY MANAGEMENT

“Glucose-lowering medications may affect weight in individuals with type 2 diabetes who are overweight or obese. Consider the effects of antihyperglycemic medications on weight before prescribing.Minimize where possible the medications for comorbid conditions that are associated with weight gain.Among selected individuals with type 2 diabetes and BMI ≥27 kg/m2”.

“Weight loss medications may be effective as adjuncts to diet, physical activity, and behavioral counseling. The potential benefits of these medications must be balanced against potential risks.”

“If an individual who was prescribed weight loss medications does not lose >5% body weight after 3 months, orexperiences safety or tolerability issues.

Discontinue the medication. Use an alternative medication or treatment approach.”

BARIATRIC SURGERY IN TYPE 2 DIABETES

“Bariatric surgery may be considered for adults with type 2 diabetes whose BMI is >35 kg/m2. In particular in individuals in whom their diabetes or associated comorbidities are difficult to control with lifestyle andpharmacologic therapy”

“Lifelong support and monitoring are necessary.There is insufficient evidence to recommend bariatric surgery for individuals with BMI ≤35 kg/m2 outside of a researchprotocol.”

ADVANTAGES OF BARIATRIC SURGERY

“Achieves near or complete normalization of glycemia2 years after surgery

Younger age, shorter diabetes duration, lower A1C,higher insulin levels, and non-use of insulin areassociated with higher post-surgery remission rates.”

DISADVANTAGES OF BARIATRIC SURGERY

• Costly

• Outcomes are variable based on the procedure and experience

of the surgeon

• Long term:

• Dumping syndrome

LIPID MANAGEMENT

STATINS

“Drugs of the statin class are structurally similarhydroxymethylglutarylÐcoenzyme A (HMG-CoA),a precursor of cholesterol,

and are competitive in hibitors of HMG-CoA reductase, the last regulatedstep in the synthesis of cholesterol

These drugs lowerserum LDL cholesterol concentrationsby upregulatingLDL-receptor activity as well as reducingthe entry of LDL into the circulation".

"Givenalone for primary or secondary prevention of heartdisease, these drugs can reduce the incidence of coronaryartery disease andreduce the risk of death from any cause by about 30percent."

"Therapy with a statin also reduces therisk of angina pectoris and cerebrovascular accidentsand decreases the need for coronary-artery bypassgraftingand angioplasty".

LIPID-ALTERING EFFECTS

"The dose required tolower serum LDL cholesterol concentrations to asimilar degree varies substantially among the statins.In addition, the response to increases in the dose isnot proportional, because the doseResponse relationfor all six statins is curvilinear In general, adoubling of the dose above the minimal effectivedose decreases serum LDL cholesterol concentrationsby an additional 6 percent. The maximal reduction In serum LDL cholesterol concentrations induced without increasing adverse effects. Combinationtherapy also reduces serum triglyceride andremnant lipoprotein concentrations, raises serum.HDL cholesterol concentrations, and improves theLDL-subclass profile109 more than does monotherapy."

ADVERSE EFFECTS

“The predominant adverse effect of nicotinic acidis flushing of the skin, an effect that about 10 percentof patients find intolerable (Table 5). The administrationof 325 mg of aspirin 30 to 60 minutesbefore each dose of nicotinic acid reduces the severityof flushing, and the aspirin can often be discontinuedafter a few days as tachyphylaxis develops inresponse to the prostaglandin-mediated flush. Patientscan also minimize flushing by taking nicotinic acidat the end of a meal and by not taking it with hotliquids. With the use of these precautionary measures,nicotinic acid can be started at a moderate dose,such as 250 to 500 mg twice daily, depending onthe patients size. The daily dose can be increased amonthly intervals by 500 or 1000 mg, to a maximumof 3000 mg, if serum aminotransferase, glucose, anduric acid concentrations do not increase excessively.”

“With each increase in the dose, flushing may recur.Other adverse effects include conjunctivitis, nasalstuffiness, loose bowel movements or diarrhea, acanthosisnigricans, and ichthyosis. Hepatitisis more frequent in patients who are taking nicotinicacid than in those who are taking statins, especiallyat doses of more than 2000 to 3000 mg of nicotinicacid daily. The symptoms and time course of nicotinic-acidÐinduced hepatitis are similar to those associatedwith statins”.

“Timed-release formulations of nicotinic acid aredesigned to minimize cutaneous flushing. However,the absence of flushing may indicate poor gastrointestinalabsorption. Other drawbacks of such formulations are hepatotoxicity at doses of 2000 mgper day or higher and smaller decreases in serumtriglyceride concentrations and smaller increasesin serum HDL cholesterol concentrations thanare

induced with plain nicotinic acid.Nonetheless,some timed-release formulations are useful inpatients who cannot tolerate plain nicotinic acid andare equivalent to plain nicotinic acid with respect tothe effects on serum lipid and aminotransferase concentrations".

Indications

"The changes in serum triglyceride and HDL cholesterolconcentrations that are induced by nicotinicacid are curvilinear, whereas the changes in serumLDL cholesterol concentrations are linear."

"Thus, a daily dose of 1500 to 2000 mg of nicotinicacid will substantially change the serum triglycerideand HDL cholesterol concentrations without causing many of the mucocutaneous and hepatic adverse effectseen with higher doses. This dose is often idealfor patients with familial combined hyperlipidemia".

"These patients usually need to take a statin as well,and because it is tolerated better, the statin should begiven first. The patients may then be more receptiveto moderate doses of plain or timed-release nicotinicacid. Higher doses of nicotinic acid (3000 to 4500mg daily) may be needed to reduce serum LDL cholesterolconcentrations substantially in patients withfamilial hypercholesterolemia even when statins anda bile-acidÐbinding resin are given concomitantly".

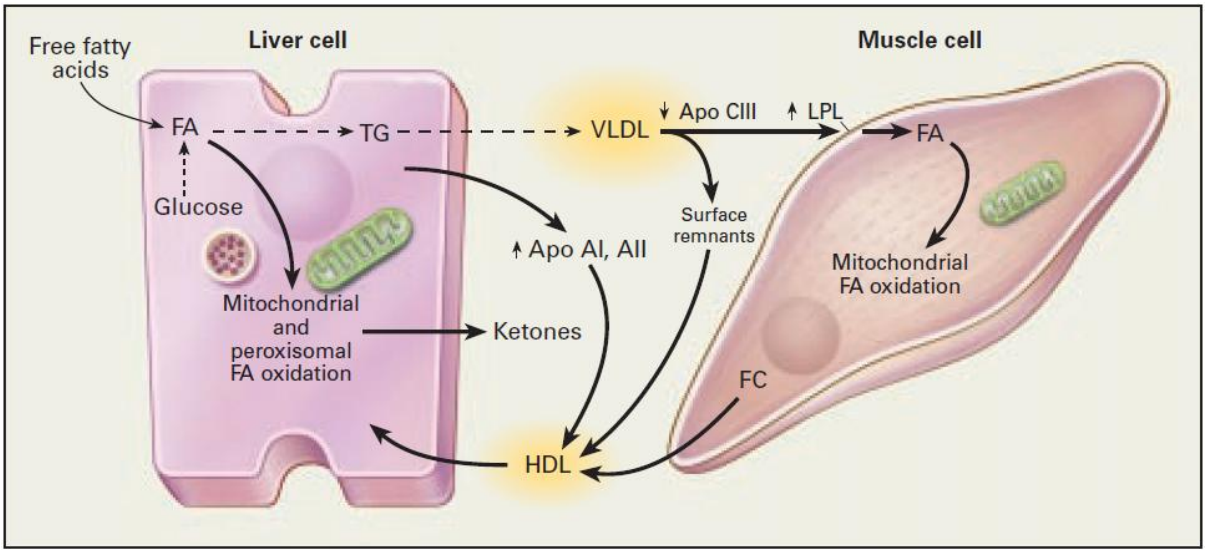
FIBRATES

Lipid-Altering Effects

"The prototypical fibric acid is clofibrate (ethyl*p*-chlorophenoxyisobutyrate). Clofibrate and relateddrugs resemble, in part, short-chain fatty acids andincrease the oxidation of fatty acids in both liver andmuscle. The increase in fatty-acid oxidation in the liver is associated with increased formation ofketone bodies (an effect that is not clinically important) and decreased secretion of triglyceride-richlipoproteins. In muscle, the increase in fatty-acid oxidationis associated with an increase in both lipoproteinlipase activity and the uptake of fatty acids."

"These drugs act by activating the nuclear transcriptionfactor peroxisome proliferator-activated receptor*a* (PPAR*a*), up-regulating the expression of theLDL cholesterol and apolipoprotein AI genes, anddown-regulating the expression of the apolipoproteinCII gene."

"The fibrates are the most effective triglycerideloweringdrugs. Patients with very high serum triglycerideconcentrations have low serum LDL cholesterolconcentrations, and these may increase duringtreatment with a fibrate. If the increase is substantial,a low-dose statin may be added to the regimen. Conversely,in patients with high serum LDL cholesterolconcentrations and moderately high serum triglycerideconcentrations, fibrates can lower serum LDLcholesterol concentrations. Fibrates also increasethe buoyancy of LDL particles, a potentially favorableeffect.Fenofibrate, which was recently approved foruse in the United States, may lower serum LDL cholesterolconcentrations more effectively than doesclofibrate or gemfibrozil.



treatment with gemfibrozil reduced the frequencyof heart disease in a placebo-controlled study of patientswith high serum VLDL and LDL cholesterolconcentrations121 and in a secondary-prevention trialin men with low serum HDL cholesterol concentrations."

"Treatment with clofibrate produced similarresults. Treatment with bezafibrate and gemfibrozilis also associated with regression of coronaryartery disease on angiography."

ADVERSE EFFECTS

"Of the three fibrates that are available in the UnitedStates, clofibrate and fenofibrate cause fewer gastrointestinal symptoms than gemfibrozil. Other adverseeffects include erectile dysfunction, especially in mentreated with clofibrate, and myositis in patients withimpaired renal function. The fibrates are largely excretedby the kidney and therefore accumulate in theserum in patients with renal failure. Because fibratesdisplace warfarin from albumin-binding sites,patients who are taking a fibrate may need up to30 percent less warfarin. All the fibrates increasebiliary

cholesterol concentrations and can cause gallstones. In one placebo-controlled study, themortality rate was increased among patients whowere receiving clofibrate, as a result of diseases of thebiliary tract and cancer. There was no increase inthe risk of death or cancer among patients who weretreated with clofibrate in another study or amongthose who received gemfibrozil".

INDICATIONS

"The primary indications for fibrate therapy are serumtriglyceride concentrations of more than 1000mg per deciliter (11.5 mmol per liter), remnant removaldisease, and low serum HDL cholesterol concentrations.
However, they may also be useful in patientswith combined hyperlipidemia."

OTHER THERAPIES

"Dietary supplementation with soluble fiber, suchas psyllium husk, oat bran, guar gum and pectin, andfruit and vegetable fibers, lowers serum LDL cholesterol concentrations by 5 to 10 percent.Sitostanol,a plant sterol incorporated into margarine,inhibits gastrointestinal absorption of cholesterol."

"The nÁ3 fatty acids can lower serum triglycerideconcentrations by up to 30 percent at a daily dose of3 g and by about 50 percent at a daily dose of 9 g."

"In postmenopausal women, oral estrogen therapy can lower serum LDL cholesterol concentrations byapproximately 10 percent and raise serum HDL cho-triples, and there is no overall reduction in therisk of recurrence of coronary disease among women."

Women with serum triglyceride concentrationsabove 300 mg per deciliter (3.4 mmol per liter)should be treated with transdermal estrogen. Rarely,an anabolic steroid such as oxandrolone or stanozololis used to reduce the hepatic secretion of triglycerides.

In patients with severe hypercholesterolemia,apheresis with dextran sulfate can be used to trap lipoproteins containing apoprotein B.

Adults not taking a statin • Obtain a lipid profile

• At diabetes diagnosis, initial medical evaluation, and every 5years thereafter

• At initiation of statin therapy and periodically thereafter

Lifestyle changes • Weight loss (if indicated)

"Reduced intake of saturated fat, trans fat, and cholesterol. Increased intake of omega-3 fatty acids, viscous fiber, and plantstanols/sterols

Increased physical activity,Intensify lifestyle changes and optimize glycemiccontrol among individuals with

• TG ≥150 mg/dL

• HDL-C <40 mg/dL (men), <50 mg/dL (women

Individuals with fasting TG ≥500mg/dL • Evaluate for secondary causes of hypertriglyceridemia.Consider medical therapy to reduce pancreatitis risk."

STATIN THERAPY FOR LIPID MANAGEMENT

"Individuals with diabetes and ASCVD* • High-intensity statin therapy + lifestyle changes"

Age <40 with diabetes and ASCVD risk factors • Moderate- or high-intensity statin + lifestyle

Age 40-75 years with diabetes but without ASCVD

risk factors

• Moderate-intensity statin + lifestyle

Age 40-75 with diabetes and ASCVD risk factors • High-intensity statin +lifestyle

Age >75 with diabetes but without ASCVD risk

factors†

• Moderate- or high-intensity statin + lifestyle

"Age >75 with diabetes and ASCVD risk factors • Moderate- or high-intensity statin + lifestyle.The intensity of statin therapy may require adjustment based on an individual's response

ASCVD Risk Factors

• LDL-C ≥100 mg/dL(2.6 mmol/L)

• High blood pressure

• Smoking

• Overweight or obesity

• Family history of premature ASCVD

*Regardless of age"

†Routinely evaluate risk-benefit profile of statin therapy, with down-titration as needed.

COMBINATION THERAPY FOR LIPID MANAGEMENT

"Statin + ezetimibe- Adding ezetimibe to moderate-intensity statin therapy has been shown to provideincremental CV benefit compared with moderate statin therapy along.This combination is a consideration for individuals.With recent ACS and LDL-C ≥50 mg/dL. Who cannot tolerate a high-intensity statin.

Statin + fibrate -This combination has not been shown to improve ASCVD outcomes. As such, it is not recommended. Statin + fenofibrate may be considered for men withTG ≥204 mg/dL and HDL-C ≤34 mg/dL."

Statin + niacin -This combination has not been shown to provide additional CV benefit above statin therapyalone.It may increase the risk for stroke. This combination is not recommended.

Statin + PCSK9 inhibitor- 36%-59% reductions have been shown with PCSK9 inhibitors on top of maximal tolerated statin therapy.

Combination statin + PCSK9 may be considered as adjunctive therapy for individuals withdiabetes who are at high ASCVD risk or who are intolerant to a high-intensity statin.

Statins & Incident Diabetes

"• Increased risk of incident diabetes with statin use has been reported.May be limited to individuals with diabetes risk factors.Analysis of initial study-cardiovascular event rate reduction with statins outweighed risk of incident diabetes

• Even for individuals at highest diabetes risk"

• Odds ratio of 1.09 for new diabetes diagnosis

CORONARY HEART DISEASE (CHD) SCREENING AND TREATMENT

SCREENING

"Routine coronary artery disease (CAD) screening in asymptomatic individuals is not recommended. It does not improve outcomes as long as ASCVD risk factors are treated.Consider investigating for CAD in the presence of: Atypical cardiac symptoms Signs or symptoms of associated vascular disease, including carotid bruits, TIA, stroke, claudiation, orPAD Electrocardiogram abnormalities."

TREATMENT

"In individuals with known ASCVD.Use aspirin and statin therapy if not contraindicated. Consider therapy with an ACEI to reduce the risk of CV events
In individuals with symptommatic heart failure:Do not use TZDs, as these agents are associated with heart failure.In individuals with type 2 diabetes and stable heart failure:Metformin may be used if renal function is normal. Metformin therapy should be avoided in unstable or hospitalized patients with heart failure."

REVIEW OF LITERATURE

IV REVIEW OF LITERATURE

1. A Comparative Study on the Fasting and the Postprandial Dyslipidaemia in Type 2 Diabetes Mellitus

LokhandeSuryabhan L, IyerChandrashekhar M, ShindeRatnendra R, NandedkarPrerna D

"This study showed significantly increased levels of serum total cholesterol, TGs, LDL-C and VLDL-C in the postprandial state as compared to those in the fasting state ($p<0.001$) and as compared to those in the fasting and the postprandial states of the controls ($p<0.001$). The serum HDL-C level was significantly lower in the postprandial state as compared to that in the fasting state ($p<0.001$). Also, the postprandial and the fasting HDL-C levels were significantly lower as compared to the levels in their respective control groups ($p<0.001$). The findings of the present study indicated that the lipid profile, as a cardiovascular risk factor, was significantly elevated in the postprandial state as compared to that in the fasting state and that it was significantly elevated in the postprandial and the fasting states in the Type 2 DM patients as compared to the levels in their respective control groups."

2. Postprandial Dyslipidemia: Emerging Lipid Profile for Cardiovascular Disease risk in Type 2 Diabetes Mellitus Subjects: A Case Control Study

LokhandeSuryabhan L MD (Biochemistry)., Gadpal Rahul R MD(Biochemistry),MeshramRevatdhamma J MD(Paediatrics), IyerChandrashekar M MD(Biochemistry)

"This study showed significantly increased levels of postprandial serum total cholesterol, TGs, LDL-C and VLDL-C as compared to those in the fasting state ($p<0.001$). The serum HDLC level was significantly lower in the postprandial state as compared to that in the fasting state ($p<0.001$). the study indicated that postprandial lipid profile, as a cardiovascular risk factor, was significantly elevated as compared to lipid profile in fasting state. This signifies that the routine estimation of the postprandial lipid profile, in addition to the fasting lipid parameters is mandatory in the cardiovascular disease risk assessment in Type 2 Diabetes Mellitus subjects."

3. Postprandial Lipid Abnormalities in Type 2 Diabetes Mellitus

SV Madhu, V Mittal , B Krishna Ram, DK Srivastava

"The present study clearly demonstrates an altered postprandial (PP) response of serum triglycerides (Tg) following oral fat challenge in male type 2 diabetes subjects compared to controls. The PP hypertriglyceridaemia remained significant

even after adjusting for fasting Tg levels and was present despite similar fasting Tg levels in diabetic patients and controls."

4. Postprandial Triglyceride rich Lipoproteins in Insulin Resistance and Type 2 Diabetes

NiinaMatikainen; MarjaRiittaTaskinen

"A prospective study of initially healthy US women included measurements of nonfasting TG concentrations of 6391 subjects with followup for a median of 11.4 years for incident cardiovascular events (myocardial infarction, ischemic stroke,bcoronary revascularization or cardiovascular death). In contrast to fasting TG, nonfasting TG levels maintained a strong independent relationship with cardiovascular events in a fully adjusted model for increasing tertiles of TG levels with the following hazard ratios: 1.00, 1.44 (95% CI: 0.902.29), and 1.98 (95% CI: 1.213.25). Another prospective cohort study of 7587 women and 6394 men from the general population of Copenhagen with followup for 26 years came to similar conclusions. The multifactorially adjusted hazard ratios increased significantly for each category per 1mmol/ l increase in nonfasting TG among both men and women. Importantly, the levels of remnant lipoprotein (RLP) cholesterol increased significantly with increasing levels of nonfasting TGs. In these prospective population cohorts, nonfasting TGs were associated with cardiovascular events and death, independent of traditional cardiac risk factors, levels of other lipids and markers of insulin resistance; by contrast, fasting TG showed little independent relationship."

5. Postprandial dysmetabolism and cardiovascular disease in type 2 diabetes

M E Tushuizen, M Diamant, R J Heine

"In diabetic patients, most emphasis was laid on hyperglycaemia, whereas recent evidence demonstrates the importance of dyslipidaemia, in particular hypertriglyceridaemia, as a cardiovascular disease risk factor. Although at present, epidemiological and long term intervention studies are largely lacking, in vivo data convincingly show an association between postprandial TRL and indicators of cardiovascular disease. Similar to postprandial hyperglycaemia, both in vivo and in vitro studies indicate that (postprandial) increases in triglycerides are proinflammatory, prothrombotic, and adversely affect several endothelial functions, by inducing oxidative stress (fig 2). Therefore, it is feasible that prolonged postprandial hypertriglyceridaemia leads to an atherogenic environment in vivo. However, as for postprandial hyperglycaemia the evidence for postprandial hypertriglyceridaemia as independent in cardiovascular disease is still scanty. More evidence, which can only be obtained from large prospective studies, is certainly required."

MATERIALS AND METHODS

V MATERIALS AND METHODS

The study was conducted in Government Rajaji Hospital, Madurai during a period of March 2016 To August 2016.The aim of the study was to study the fasting and post prandial lipid levels in patients with type 2 diabetes mellitus and to assess the significance of post prandial dyslipidemia with respect to fasting dyslipdemia as cardiovascular risk factor in these patients.This study comprised of 100 patients in study group and 100 healthy subjects in control group.

STUDY POPULATION:

The study was conducted on patients from General Medicine ward and Diabetology OPD of GovernmentRajaji Hospital, Madurai during the period of March 2016 To August 2016

INCLUSION CRITERIA:

All patients with diabetes mellitus diagnosed according to World Health Organization (WHO) criteria

-onset of diabetes after 30 years

-duration more than or equal to 5 years in General Medicine wards and attending Diabetology OPD of Government RajajiHospital,Madurai.,

EXCLUSION CRITERIA:

Patients with

-history of lipid disorder

-history of hypertension

-history or electrocardiography (ECG) evidence of CAD

-history of heart failure

-history of renal dysfunction

-history of liver disease

-history of stroke

-history of GI surgery

-history or features of hypothyroidism,

-history of drug intake affecting lipid metabolism.

CONTROL GROUP: Age and sex matched 100 healthy subjects were selected after getting informed consent. The same exclusion criteria were applied to control group also.

A predesigned proforma was used to collect the demographic and clinical details of the patients and the controls.

History regarding diabetes ,duration of diabetes,age at which diabetes was diagnosed were asked.

History regarding past history of HT / GI surgery / stroke/ CKD / cardiac disease, history of pregnancy / lactation, history of any chronic drug intake, family history of DM / HT / CADwas enquired.

Clinical examination of height, weight, blood pressure, heart rate pulse rate was done for all patients. Abdominal obesity was measured by waist hip ratio. Waist circumference were measured at the midpoint of the costal marginand the top of the iliac crest, using a stretch-resistant tape . Hip circumference weremeasured , with the tape parallel to the floor ,at the widest portion of the buttocks. The subject was made to stand with feet close together .The measurements were taken at the end of a normal expiration. Each measurement were repeated twice.forprecision.WHR>.90 in men and WHR>.80 in women were taken as having significant cardiovascular risk.

12 lead ECG and TTE will be done for assessing the cardiovascular status.

Laboratory investigations like complete hemogram, RFT, LFT, urine routine, Fasting Blood Sugar, 2hr Post Prandial Blood sugar, fasting lipid profile and 6 hr post prandial weredonefor study group and control group.

RESULTS

VI RESULTS

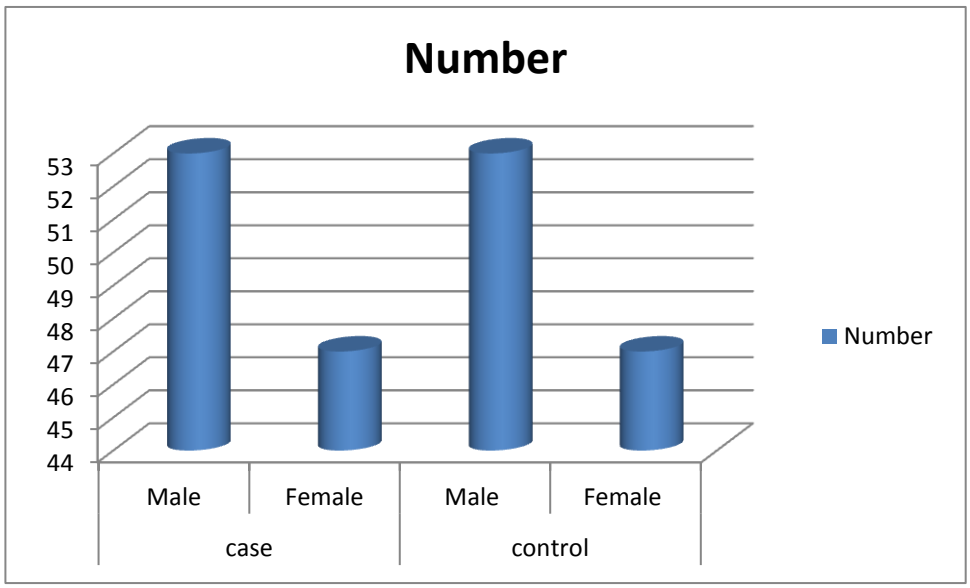
SEX DISTRIBUTION

The study population for type 2 Diabetes mellitus consisted of100 patients(53 males and47 females) and the control groupconsisted of 100 subject (53 males and 47 females).

Table 1 Sex distribution for type 2 diabetes mellitus in cases andcontrols

	case		control	
	Male	Female	Male	Female
Number	53	47	53	47

Chart 1 Sex distribution for type 2 diabetes mellitus in cases andcontrols



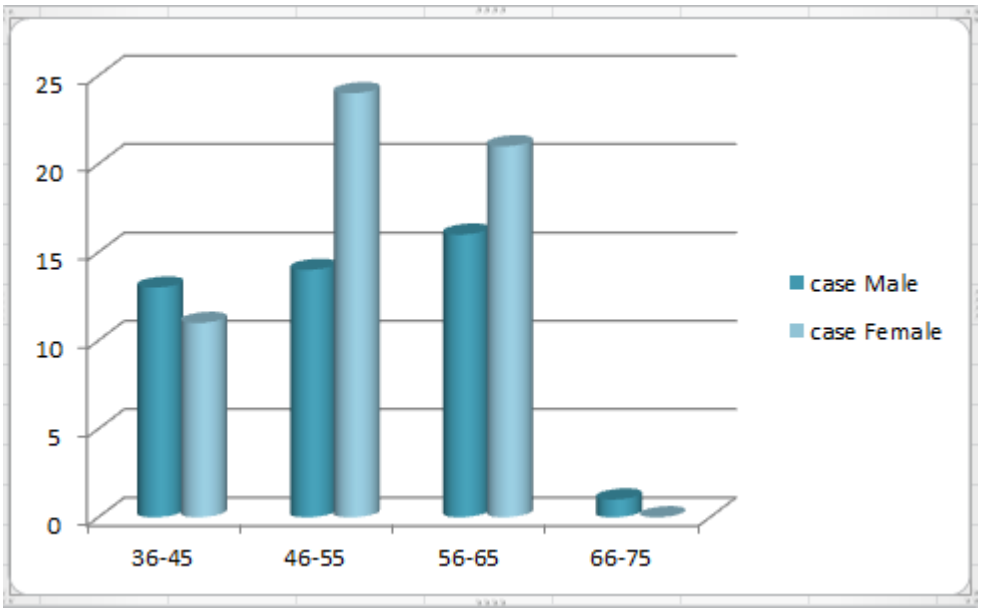
AGE DISTRIBUTION

The Type 2 diabetes cases were in the age group of 36 — 75 years. 24% ofthe cases were in the age group of 36— 45 years,38%to age group 46— 55 years,37% to the age group 56-65 years. 1% were between 66-75years.

Table 2 Age distribution for Type 2 DM cases

Age in years	case	
	Male	Female
36-45	13	11
46-55	14	24
56-65	16	21
66-75	1	0

Chart 2 Age distribution for Type 2 DM cases



BLOOD GLUCOSE LEVELS IN STUDY GROUP (TYPE 2 DM) AND CONTROLS

The average blood glucose levels of fasting and post prandial in the diabetic subjects were 168.94 mg/dl and 237.15 mg/dl respectively. In control population th average 116.94mg/dl.

	Average FBS mg/dl	Average PPBS mg/dl
Case	168.94	237.15
control	92.19	116.94

Table 3-Average Blood glucose levels in study group (Type 2 DM) and Controls

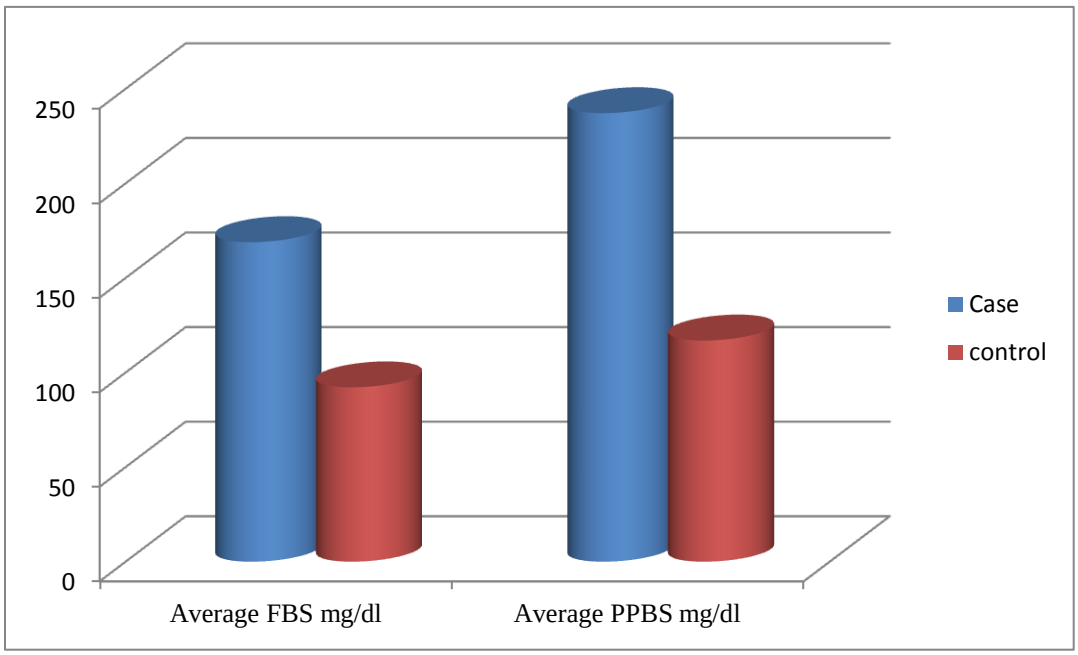


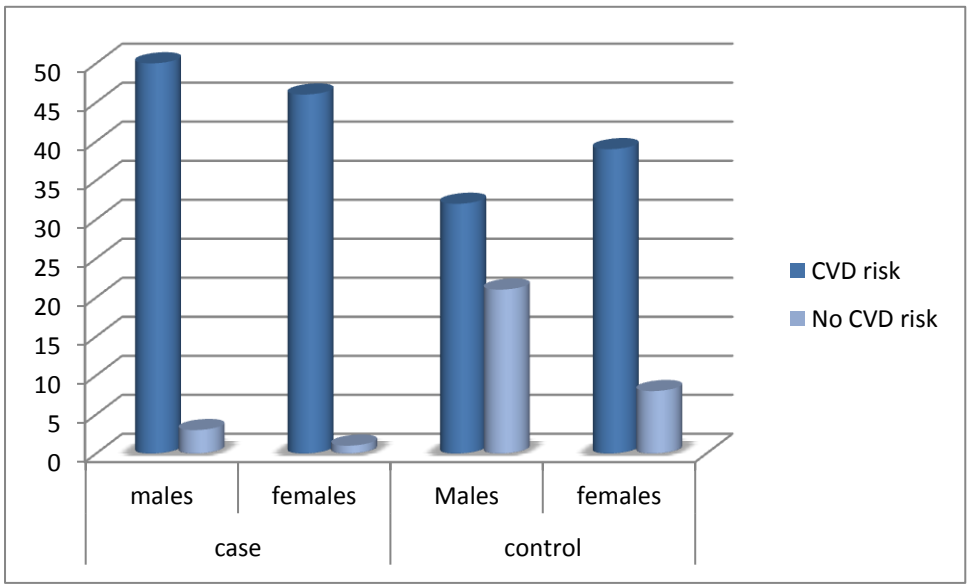
Chart 3-Average Blood glucose levels in study group (Type 2 DM) and Controls

CARDIOVASCULAR RISK IN TYPE 2 DIABETES MELLITES

Among the100 cases of Type2 Diabetes mellitus,96 had cardiovascular risk . Of these 96 cases,50 were male patients and 46 were females.by taking value of WHR 0.90 for males and 0.8. for females ,the cardiovascular risk was assessed.in control population among 100 people 71 had cardiovascular risk with 32 being males and 39 being females.

	case		control	
	males	females	Males	females
CVD risk	50	46	32	39
No CVD risk	3	1	21	8

Table4 Cardiovascular risk in type2 diabetic patients and controls



Char4 Cardiovascular risk in type2 diabetic patients and controls

FASTING AND POSTPRANDIAL LIPID PROFILE IN STUDY POPULATION

The fasting lipid profile was measured for the study and control population ,the average values of the fasting levels for the study group were TC of 212.77mg/dl,TG of 156mg/dl,LDL of 132.07mg/dl and HDL of 43.18mg/dl,For the control population the values were TC of 153.32mg/dl,TG of 115.31mg/dl ,LDL of 89.2mg/dl,HDL of 47.9mg/dl.

The postprandial lipid profile for the study and control population was done,the average values for the study group were TC of 236.33mg/dl,TG of 176.87mg/dl,LDL of 165.84mg/dl and HDL of 41.93mg/dl,For the control population the values were TC of 185.47mg/dl,TG of 161.26mg/dl ,LDL of 122.23mg/dl,HDL of 41.6mg/dlTable5 comparison of average fasting and postprandial lipid profile among cases and control

Table5 comparison of average fasting and postprandial lipid profile among cases and control

	FLP average		PPLP average	
	Case mg/dl	Control mg/dl	Case mg/dl	Control mg/dl
TC	212.77	153.32	236.33	185.47
TG	156	115.31	176.87	161.26
LDL	132.07	89.2	165.84	122.23
HDL	43.18	47.9	41.93	41.6

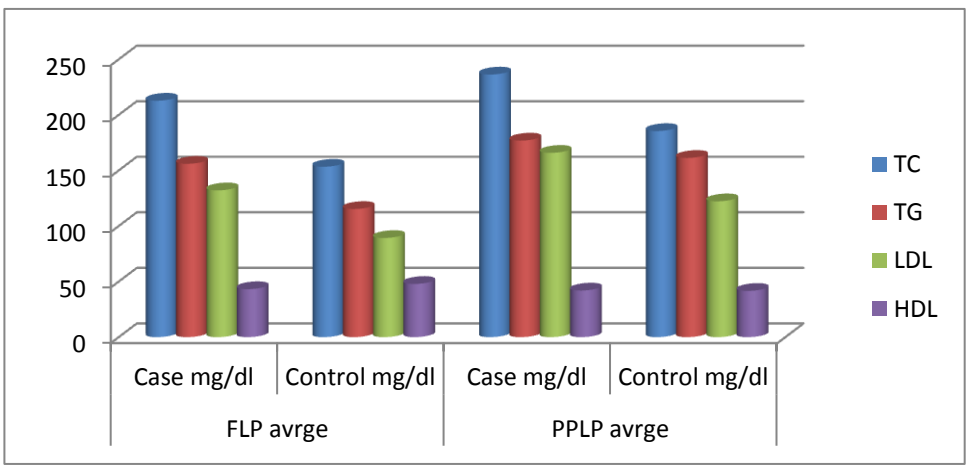


Chart5:Comparison of average fasting and postprandial lipid profile among cases and control

By comparing with the standard reference values of the lipid profile out of the 100 diabetic subjects 53 had fasting dyslipidemia out of which 29 were males and 24 were females.Out of the control subjects 21 had dyslipidemia out of which 10 were males and 11 females.

	case		Control	
	Male	Female	Male	Female
Dyslipidemia	29	24	10	11
No dyslipidemia	24	23	43	36

Table 6 comparison of prevalence of fasting dyslipidemia in cases and controls

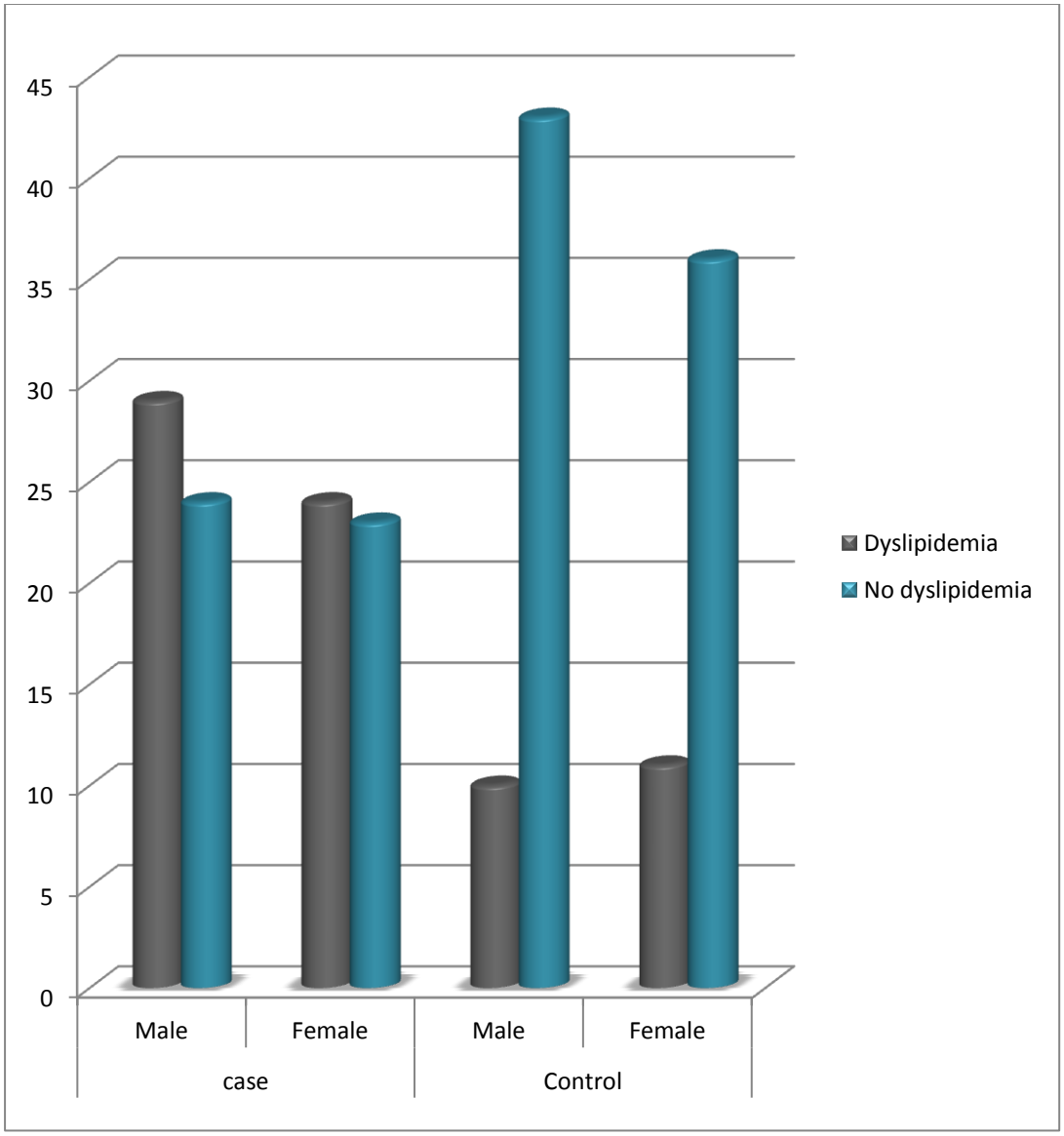


Chart 6 comparison of prevalence of fasting dyslipidemia in cases and controls

By comparing with the standard reference values of the lipid profile out of the 100 diabetic subjects 64 had post prandial dyslipidemia out of which 23 were males and 41 were females. Out of the control subjects 43 had dyslipidemia out of which 29 were males and 14were females

Table 7 Comparison of postprandial dyslipidemia in type2 diabetic patients and controls

	case		Control	
	Male	Female	Male	Female
Dyslipidemia	23	41	29	14
No dyslipidemia	30	6	24	22

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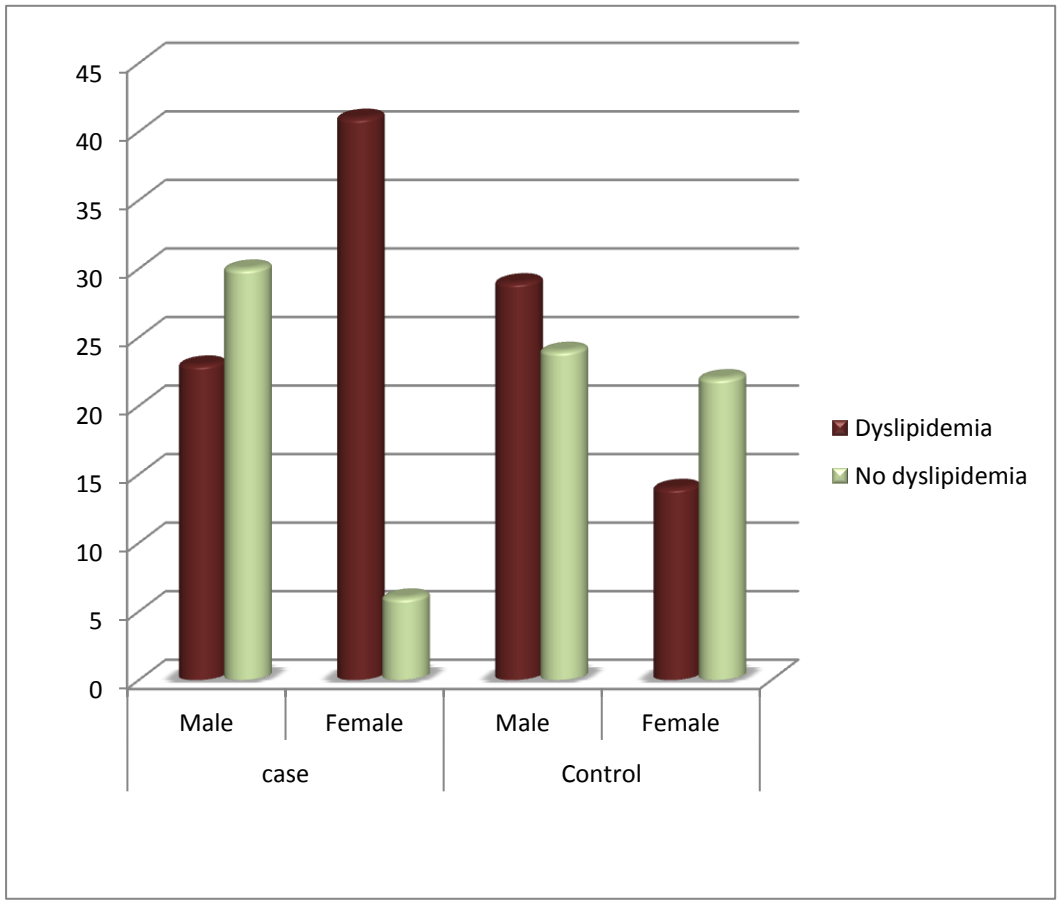
Chart 7 Comparison of postprandial dyslipidemia in type2 diabetic patients and controls



VII ANALYSIS OF RESULTS AND DISCUSSION

STATISTICAL ANALYSIS :

Master chart was prepared with all the information collected about the selected cases .with the help of computer Data analysis was done by using SPSS software and Sigma Stat 3.5 version (2012). Using this software, percentage, mean, standard deviation and `p' value were calculated through Student 't' test, One way ANOVA, Pearson Correlation and Chi square test and P value of < 0.05 was taken as significant.

DISCUSSION

DISCUSSION

In this studythe fasting and post prandial lipid levels in patients with type 2 diabetes mellitus was compared and the significance of post prandial dyslipidemia with respect to fasting dyslipdemia as cardiovascular risk factor in these patients was assessed.

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COMPARISON OF WAIST HIP RATIO IN DIABETIC PATIENTS AND CONTROLS

Among the100 cases of Type2 Diabetes mellitus,by taking value of WHR 0.90 for males and 0.8. for females ,the cardiovascular risk was assessed..96 had cardiovascular risk .Of these 96 cases,50 were male patients and 46 were females. In control population among 100 people 71 had cardiovascular risk with 32 being males and 39 being females We observed that the waist to hip ratios of the diabetic males and females were found to be statistically significant ($p<0.05$) as compared to those of their respective controls

Subjects	Waist hip ratio (Mean ± SD)		
	Cases (n=100)	Controls (n=100)	p value
Males	0.95±0.038	0.91±0.023	0.000*
Females	0.86±0.037	0.83±0.037	0.000*

Table 8 Comparison of waist hip ratio in diabetic patients and controls

CORRELATION OF VALUES OF FASTING AND POSTPRANDIAL BLOOD GLUCOSE LEVELS IN STUDY GROUP (TYPE 2 DM) AND CONTROLS

Fasting and post prandial average blood glucose levels were 168.94 mg/dl and 237.15 mg/dl respectively in the diabetic subjects. In control population th average fasting blood glucose was 92.19mg/dl and postprandial blood glucose was 116.94mg/dl. In this study we observed a significant increase in both fasting as well as postprandial blood glucose levels in the Type 2 Diabetic subjects, as compared to those of their respective controls. Also, the postprandial blood glucose level was significantly increased (p<..05)as compared to that in the fasting state in the Type 2 Diabetic subjects.

Table 9 Correlation of values of fasting and postprandial blood glucose levels in study group (Type 2 DM) and controls

Blood glucose levels	**Type 2 DM subjects (n=100) (Mean ±SD)**	**Controls (n=100)(Mean±SD)**	**p value**
Fasting glucose	168.94±30.61	92.19±11.03	0.000*
Post prandial glucose	237.15±40.68	115.72±17.76	0.000*
p value	0.000*	0.000*	

CORRELATION OF PARAMETERS OF FASTING LIPID PROFILE IN STUDY GROUP (TYPE 2 DM) AND CONTROL GROUP

The fasting lipid profile was measured for the study and control population ,the average values of the fasting levels for the study group were TC of 212.77mg/dl,TG of 156mg/dl,LDL of 132.07mg/dl and HDL of 43.18mg/dl,For the control population the values were TC of 153.32mg/dl,TG of 115.31mg/dl ,LDL of 89.2mg/dl,HDL of 47.9mg/dl.

We observed a significant increase in the serum total cholesterol (TC), triglycerides (TGs), the LDL-cholesterol levels in the fasting state in the Type 2 DM patients as compared to those in the control subjects ($p<0.001$). The HDL-cholesterol level was significantly decreased in the fasting state in the Type 2 DM patients ascompared to that in the control subjects ($p<0.001$).

Fasting serum lipids	Diabetics (n=100)(Mean±SD)	Controls(n=100)(Mean±SD)	p value
Total Cholesterol	212.77±41.25	157.9±20.86	0.000*
Triglyceride	156.57±45.37	115.31±35.43	0.000*
HDL	43.18±8.97	47.9±6.49	0.000#
LDL	132.07±34.5	89.26±10.72	0.000*

Table 10 Correlation of parameters of fasting lipid profile in study group (type 2 dm) and control group

CORRELATION OF VARIOUS PARAMETERS OF POSTPRANDIAL LIPID PROFILE IN STUDY GROUP (TYPE 2 DM)

The postprandial lipid profile for the study and control population was done,the average values for the study group were TC of 236.33mg/dl,TG of 176.87mg/dl,LDL of 165.84mg/dl and HDL of 41.93mg/dl,For the control population the values were TC of 185.47mg/dl,TG of 161.26mg/dl ,LDL of 122.23mg/dl,HDL of 41.6mg/dl.

We observed a significantpostprandial state increase in the serum total cholesterol (TC), triglycerides (TGs) and the LDL-cholesterol levels in the Type 2 DM patients as compared to those in the control subjects ($p<0.001$). But the HDL-cholesterol level was not significantly decreased in the postprandial state in the Type 2 DM patients as compared to that in the control subjects ($p=0.770$)

Post prandial serum lipids	Diabetics (n=100)(Mean±SD)	Controls(n=100)(Mean±SD)	p value
Total Cholesterol	236.33±39.44	185.47±27.99	0.000
Triglyceride	176.87±48.68	161.26±19.74	0.003
HDL	41.93±8.57	41.6±7.38	0.770
LDL	165.84±37.48	122.23±43.83	0.000

Table 11 Correlation of parameters of postprandial lipid profile in study group (type 2 dm) and control group

VALUES OF VARIOUS PARAMETERS OF FASTING AND POSTPRANDIAL LIPID PROFILE IN STUDY GROUP.

We observed a significant increase in the serum total cholesterol (TC), triglycerides (TGs), the LDL-cholesterol levels in the postprandial state in the Type 2 DM patients as compared to their serum levels in the fasting state ($p<0.001$). but in our study the HDL-cholesterol level was not significantly decreased in the postprandial state as compared to that in the fasting state in the Type 2 DM patients ($p=.314$)

Type 2 DM subjects (n=100)	Fasting lipid profile	Post prandial lipid profile	p value
Total Cholesterol	212.77±41.25	236.33±39.44	0.000[Y]
Triglyceride	156.57±45.37	176.87±48.68	0.002 [Y]
HDL	43.18±8.97	41.93±8.57	0.314
LDL	132.07±34.5	165.84±37.48	0.000 [Y]

Table 12. Values of various parameters of fasting and postprandial lipid profile in study group

CONCLUSION

CONCLUSION

Atherosclerosis is a postprandial phenomenon with respect to lipids, as we are in the postprandial phase for most of the day, with an additional adverse effect of the meal induced hyperglycaemia. The present study suggests that it is important to routinely estimate the postprandial lipid profile, in addition to the fasting lipid parameters, in the cardiovascular risk assessment in Type 2 DM. Thus, by rectifying the abnormal postprandial lipid parameters early in the course of diabetes, we can prevent the hazardous complications which are associated with Type 2 DM, the most common one being atherosclerotic coronary artery disease.

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PROFORMA

Name:

Age / Sex:

IP no:

Occupation:

Presenting complaints:

Past History:

Personal history

alcoholic/ non alcoholic

smoker/ nonsmoker

Clinical Examination:

General Examination: Consciousness, orientation,febrile/afebrile, Pallor, jaundice, Clubbing, Lymphadenopathy, pedal edema.

Vitals:

PR

BP

RR

SPO2

Systemic examination:

CVS:

RS:

ABDOMEN:

CNS:

Laboratory investigations:

FBS

PPBS

FLP-TC TG LDL HDL

PPLP-TC TG LDL HDL

Diagnosis

MASTER CHART

CASE

AGE	SEX	WHR	FBS	PPBS	FTC	FTG	FLDL	FHDL	PPTC	PPTG	PPLDL	PPHDL
36	F	0.83	205	224	251	108	159	41	276	246	184	43
37	F	0.82	166	256	195	138	134	34	281	167	222	38
37	M	0.97	202	234	204	103	153	42	226	213	178	45
38	M	0.98	140	256	206	109	124	42	175	114	102	38
38	F	0.93	119	287	231	125	130	48	288	165	195	54
39	F	0.86	193	223	202	194	146	43	248	185	167	46
39	M	0.93	169	255	215	209	89	23	298	275	201	30
40	F	0.9	114	194	256	102	134	63	283	165	188	56
40	M	0.96	195	223	209	138	176	44	235	256	122	52
41	M	0.93	188	275	222	103	87	47	241	175	175	45
41	M	0.98	193	214	187	234	100	32	224	165	157	45
42	F	0.89	143	223	206	102	142	53	253	195	146	56
43	F	0.81	143	266	225	194	103	53	235	136	185	23
43	M	0.92	220	281	288	101	172	45	298	263	202	32
43	M	0.96	148	195	195	192	98	45	241	267	136	49
43	F	0.83	168	222	206	166	188	55	267	154	188	52
43	M	0.94	184	177	206	102	104	52	254	210	188	43
43	F	0.89	178	146	178	224	104	29	273	104	249	24
44	M	0.93	231	247	265	231	162	42	213	166	146	45
44	M	0.95	195	291	268	202	198	56	246	176	157	54
44	M	0.98	158	285	186	87	128	43	264	246	176	44
44	F	0.96	167	190	163	211	108	36	205	154	145	32
44	F	0.85	106	267	284	154	77	53	302	165	248	34
45	M	0.96	173	214	264	104	172	54	264	127	198	55
46	F	0.85	211	250	236	139	154	43	193	176	126	47
46	M	1.02	188	211	217	127	164	48	223	197	154	47
46	M	0.94	146	196	214	91	93	35	265	167	206	36
47	F	0.89	136	236	172	143	109	39	199	128	138	43
47	M	0.95	124	275	137	98	88	28	194	112	142	44
47	F	0.92	219	224	206	111	154	45	198	167	124	36
47	M	0.92	138	197	178	183	187	34	214	156	134	39
47	F	0.82	175	286	164	203	107	32	231	213	173	43
47	M	0.88	138	267	189	188	178	32	210	145	157	36
48	M	0.96	194	258	180	189	116	28	186	213	124	26
48	M	0.94	154	212	168	115	112	32	247	137	197	37
48	M	0.92	266	317	246	128	129	54	299	168	196	56
49	M	0.95	240	322	318	210	105	63	187	164	128	56

49	M	0.92	183	213	194	206	128	43	265	163	186	45
49	F	0.9	172	344	302	128	143	54	300	135	241	44
49	F	0.86	194	316	306	231	112	54	298	173	207	60
49	M	0.93	168	231	198	103	162	37	254	116	205	33
49	M	1.08	149	163	175	155	104	32	198	196	132	37
50	F	0.86	166	298	195	127	143	36	245	147	193	34
50	M	0.99	186	195	177	212	98	31	214	157	156	36
50	M	0.96	187	233	261	209	165	53	199	256	117	34
50	F	0.89	167	246	226	102	168	46	254	174	198	45
51	M	0.91	195	224	187	195	93	43	276	165	194	46
51	M	0.93	193	208	211	167	108	53	243	340	138	51
51	M	0.97	189	190	193	132	199	49	199	115	123	54
52	M	0.92	178	267	217	100	137	43	278	175	202	42
52	F	0.83	189	198	249	217	73	34	284	184	214	34
53	F	0.93	192	285	168	174	156	39	226	156	168	34
53	F	0.88	137	168	173	129	146	34	178	118	125	40
53	M	0.96	92	244	284	175	148	57	188	134	124	34
53	F	0.89	129	218	146	109	138	42	198	176	127	43
53	M	0.96	190	210	214	152	124	47	264	165	193	45
54	F	0.9	123	218	228	167	153	52	211	174	146	45
54	F	0.89	172	224	169	204	135	43	184	122	127	43
55	M	0.98	145	291	184	88	104	31	195	193	145	28
55	M	0.92	182	221	214	170	162	42	166	124	114	38
55	M	0.94	152	215	185	134	127	42	236	154	166	44
55	F	0.8	196	228	198	145	104	45	225	183	146	47
55	F	0.82	140	265	189	198	89	25	148	126	104	28
56	M	0.98	156	195	178	173	124	38	234	234	166	36
56	F	0.86	194	277	293	241	91	42	296	114	239	34
57	F	0.84	182	165	192	143	105	36	187	224	102	40
57	M	0.99	159	283	278	189	143	46	231	186	168	44
57	M	0.94	185	263	202	167	149	64	256	247	143	59
57	F	0.84	140	211	248	176	82	53	287	265	188	50
57	M	0.98	145	281	212	187	103	51	287	175	218	54
58	F	0.87	178	296	168	112	122	28	231	132	184	32
58	F	0.84	199	261	167	230	112	36	168	129	116	32
58	F	0.84	138	256	185	102	104	43	257	154	184	48
58	F	0.84	147	272	226	187	87	54	254	187	152	55
58	M	0.96	160	193	175	98	125	54	136	194	74	55
58	F	0.86	199	231	245	221	149	46	284	136	226	45
58	M	0.97	184	214	198	221	103	51	253	145	182	46
59	M	0.81	166	215	197	115	184	24	224	320	136	28

59	F	0.81	169	206	222	152	94	57	254	134	175	54
60	F	0.88	188	257	212	139	106	40	214	237	166	38
60	F	0.86	159	233	245	239	164	44	213	176	134	34
60	M	0.92	160	285	241	123	187	42	244	165	188	33
60	F	0.82	173	185	202	112	118	44	262	298	176	49
61	F	0.86	156	267	186	156	193	34	231	145	165	36
61	M	0.89	186	198	203	92	98	52	256	278	142	34
61	F	0.83	192	213	120	183	82	52	165	145	107	44
62	F	0.93	167	216	289	104	146	54	184	165	108	50
62	M	0.95	139	231	211	116	192	39	234	175	178	36
63	F	0.86	177	285	184	112	106	42	188	164	128	49
63	M	0.91	167	246	275	163	196	47	163	126	112	35
63	F	0.88	137	143	189	100	188	42	223	225	132	47
63	F	0.87	172	285	184	156	96	42	256	116	184	40
63	F	0.81	185	260	213	190	198	42	197	165	129	32
64	M	0.94	187	260	214	209	136	43	298	136	216	42
64	F	0.83	186	216	199	198	145	36	267	147	204	33
64	M	0.98	204	281	361	220	222	54	265	112	192	54
64	M	0.99	135	146	178	235	88	36	268	174	208	33
65	M	0.94	91	219	196	103	135	36	267	165	206	30
65	M	0.93	103	233	217	133	129	41	283	221	217	44
68	M	0.98	136	228	192	173	102	38	254	223	194	43

CONTROL

AGE	SEX	WHR	FBS	PPBS	FTC	FTG	FLDL	FHDL	PPTC	PPTG	PPLDL	PPHDL
32	M	0.9	96	110	102	81	65	35	176	158	98	33
32	M	0.95	91	112	122	73	88	39	245	157	154	38
36	M	0.95	106	120	122	75	68	46	194	184	97	42
37	F	0.81	97	136	123	88	78	43	213	186	99	47
37	M	0.9	74	132	126	96	72	63	199	165	144	41
37	M	0.88	77	109	127	112	96	48	241	185	92	37
37	M	0.94	98	103	128	78	74	44	164	164	128	34
37	M	0.93	107	109	128	96	78	36	184	195	154	24
37	M	0.92	93	100	133	114	73	48	166	166	98	38
38	F	0.82	98	108	134	74	93	56	185	134	11	38
39	F	0.81	91	148	136	73	92	45	206	164	142	35
41	M	0.91	88	102	136	83	82	53	191	172	144	47

41	M	0.93	101	119	136	96	82	50	203	157	152	34
42	M	0.91	90	73	136	115	85	41	227	143	146	38
42	F	0.82	91	120	137	67	94	44	208	164	102	33
43	F	0.79	76	101	137	85	79	48	196	175	124	45
43	M	0.9	92	132	137	107	79	54	204	164	18	34
43	F	0.81	84	89	137	126	71	49	144	156	95	45
43	M	0.9	88	94	138	65	93	39	138	155	99	51
44	M	0.93	86	123	138	115	72	49	166	194	123	38
44	M	0.89	76	102	139	102	92	35	204	185	99	38
44	F	0.82	102	103	139	148	79	53	167	144	147	35
44	M	0.92	106	136	140	98	110	29	216	158	96	43
44	F	0.79	92	132	142	75	80	42	248	136	94	55
46	F	0.79	93	124	142	100	82	44	165	146	102	36
46	F	0.83	100	108	143	67	94	43	202	146	145	45
46	M	0.94	94	124	143	96	98	46	217	241	147	42
46	M	0.92	76	127	145	98	92	52	146	157	126	45
46	F	0.84	76	99	146	88	87	39	194	185	154	46
46	M	0.91	104	127	146	112	78	44	164	204	134	44
47	M	0.86	104	120	146	139	99	49	243	185	175	47
47	F	0.95	95	134	147	86	92	54	197	153	97	46
47	M	0.93	83	126	147	93	98	49	204	125	145	35
47	F	0.83	92	120	147	121	88	63	194	164	112	43
47	M	0.94	70	120	148	102	93	48	199	145	99	52
47	F	0.84	79	118	148	127	88	41	184	152	151	42
47	M	0.96	89	132	148	128	88	47	244	167	123	46
47	M	0.92	110	119	148	128	99	49	156	194	90	35
47	M	0.88	99	102	148	136	93	53	188	164	114	53
49	M	0.94	78	102	149	85	92	46	206	164	123	39
49	M	0.9	108	130	152	103	104	47	226	125	105	38
49	F	0.83	90	156	153	88	89	36	185	175	157	45
51	F	0.82	109	118	153	128	92	53	176	164	146	33
52	F	0.87	98	118	154	94	83	48	167	157	85	48
52	M	0.92	78	80	154	108	82	58	122	159	465	42
52	F	0.82	75	90	154	112	87	51	157	164	134	41
52	M	0.93	87	128	154	112	94	43	204	145	114	36
52	M	0.9	95	128	154	148	91	48	215	167	104	54
53	M	0.93	97	116	156	69	116	36	172	167	84	54
53	F	0.83	91	115	156	95	110	31	173	143	102	54
53	F	0.83	76	124	156	128	88	60	154	164	94	34
53	F	0.84	94	108	156	196	68	41	186	164	128	24
53	F	0.84	92	156	158	111	80	52	183	164	122	46

54	M	0.89	92	112	159	79	89	44	155	105	95	37
54	M	0.88	96	118	159	84	69	44	183	167	112	38
54	F	0.8	94	132	162	94	92	54	209	204	107	43
54	M	0.91	112	128	162	110	99	52	143	148	128	39
54	M	0.89	86	104	162	128	84	45	197	128	99	56
54	F	0.82	93	126	163	88	102	44	184	164	99	27
54	F	0.81	109	126	163	94	94	55	159	154	111	33
54	M	0.92	98	118	163	99	89	49	177	167	143	45
54	M	0.9	96	104	163	125	94	54	175	156	124	51
54	M	0.89	99	128	164	136	91	44	194	157	154	36
54	M	0.91	85	167	164	142	103	44	173	145	123	42
55	M	0.96	92	126	164	154	91	59	203	154	105	35
55	F	0.81	76	89	165	147	77	51	204	175	132	46
55	F	0.9	82	108	166	124	104	42	153	135	91	37
55	F	0.92	78	110	167	72	89	56	156	187	133	41
55	F	0.84	110	88	167	127	68	52	164	175	112	49
55	F	0.86	96	98	167	165	68	52	207	126	112	42
55	F	0.82	91	109	168	72	103	53	211	175	99	34
56	M	0.92	98	108	172	99	97	49	165	156	149	44
56	M	0.92	74	96	172	115	89	41	226	167	134	37
56	F	0.84	108	190	172	124	87	55	185	167	152	45
57	F	0.82	90	120	172	135	98	55	209	167	122	54
57	F	0.86	88	102	173	129	89	56	217	145	118	46
58	F	0.91	94	123	173	129	94	50	177	136	144	42
58	M	0.92	96	96	173	147	105	49	167	174	140	46
59	M	0.94	68	112	173	152	89	51	173	157	142	44
60	M	0.92	109	130	173	156	92	53	158	164	165	39
60	F	0.81	95	109	174	76	82	46	165	194	76	52
60	M	0.91	88	112	176	86	94	56	164	185	145	39
61	M	0.9	92	132	178	165	109	49	198	172	125	45
62	F	0.81	91	106	182	135	91	49	216	145	125	26
62	M	0.87	74	108	183	145	93	53	128	144	102	38
62	F	0.91	80	119	183	212	103	44	167	164	88	42
62	F	0.81	98	111	184	135	79	43	124	153	134	43
62	M	0.88	104	128	184	142	78	46	164	145	94	52
62	M	0.89	116	115	184	142	99	59	205	152	146	48
63	M	0.9	108	128	187	103	103	52	167	176	145	35
63	F	0.83	89	102	187	146	99	47	139	145	137	37
63	F	0.8	98	102	188	131	77	42	173	164	134	38
63	F	0.84	108	102	188	140	93	50	124	145	98	46
63	M	0.89	79	96	188	147	78	48	185	164	112	24

64	F	0.82	70	92	190	185	103	51	195	134	114	38
65	F	0.8	99	124	192	124	92	40	194	154	116	42
65	F	0.81	84	112	194	145	98	51	167	158	94	44
65	M	0.9	112	90	198	94	87	52	195	165	105	67
66	F	0.79	92	98	208	200	99	50	219	128	98	43
68	M	0.92	100	136	217	212	103	49	226	173	157	45

MADURAI MEDICAL COLLEGE
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(Affiliated to The Tamilnadu Dr.MGR Medical University, Chennai, Tamil Nadu)

ETHICS COMMITTEE CERTIFICATE

Name of the Candidate	:	Dr. Deepa K.P
Course	:	PG in MD General Medicine
Period of Study	:	2014-2017
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	A comparative study on the fasting and post prandial lipid levels as a cardiovascular risk factor in patients with type 2 diabetes mellitus
Ethical Committee as on	:	16.03.2016

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

Member Secretary Chairman Dean / Convenor

Dean,
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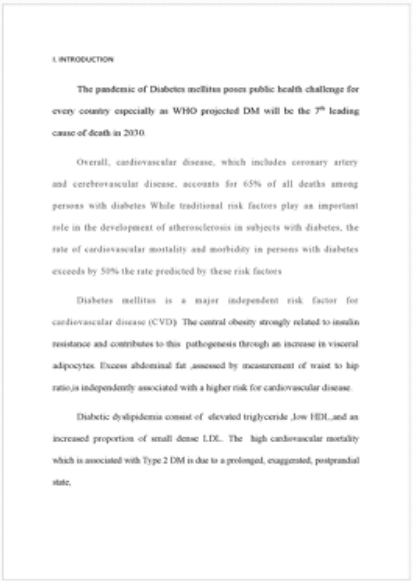

1. INTRODUCTION

The pandemic of Diabetes mellitus poses public health challenge for every country especially as WHO projected DM will be the 7th leading cause of death in 2030.

Overall, cardiovascular disease, which includes coronary artery and cerebrovascular disease, accounts for 65% of all deaths among persons with diabetes Whole traditional risk factors play an important role in the development of atherosclerosis in subjects with diabetes, the rate of cardiovascular mortality and morbidity in persons with diabetes exceeds by 50% the rate predicted by these risk factors

Diabetes mellitus is a major independent risk factor for cardiovascular disease (CVD). The central obesity strongly related to insulin resistance and contributes to this pathogenesis through an increase in visceral adipocytes. Excess abdominal fat ,assessed by measurement of waist to hip ratio,is independently associated with a higher risk for cardiovascular disease.

Diabetic dyslipidemia consist of elevated triglyceride ,low HDL,and an increased proportion of small dense LDL. The high cardiovascular mortality which is associated with Type 2 DM is due to a prolonged, exaggerated, postprandial state,

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Diabetes mellitus is a major independent risk factor for cardiovascular disease (CVD) The central obesity strongly related to insulin resistance and contributes to this pathogenesis through an increase in visceral adipocytes. Excess abdominal fat ,assessed by measurement of waist to hip ratio,is independently associated with a higher risk for cardiovascular disease.

Diabetic dyslipidemia consist of elevated triglyceride ,low HDL,and an increased proportion of small dense LDL. The high cardiovascular mortality which is associated with Type 2 DM is due to a prolonged, exaggerated, postprandial state.

The abnormal lipid profile in the postprandial state is more significant than the abnormal lipid profile in the fasting state in causing atherosclerotic complications in Type 2 diabetics

In this study, an effort is made to correlate the assess the significance of post prandial dyslipidemia with respect to fasting dyslipdemia as cardiovascular risk factor in these patients.

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